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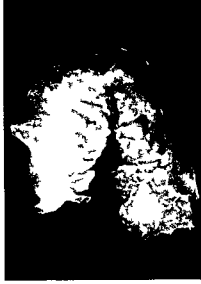
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# SURGERY

## GYNECOLOGY AND OBSTETRICS

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### JOINT DÉBRIDEMENT

#### Surgical Treatment of Degenerative Arthritis

PAUL B. MAGNUSON, M.D., F.A.C.S., Chicago, Illinois

IT has been assumed in general by the medical profession that a joint damaged as a result of any form of arthritis is beyond help, except by the eradication of any possible foci of infection which might be found or the elimination of chemical disturbances of metabolism. Certainly chemical upsets can be a contributing cause to the degenerative forms of arthritis,<sup>1</sup> as can also be foci of infection. There can be no doubt, however, that it occurs most frequently in joints which are subject to often-repeated small trauma. Bauer and Bennett<sup>2</sup> believe that "degenerative arthritis is the result of the wear and tear of increasing age and repeated trauma which may be caused in a variety of ways and that it is not the result of an inflammatory process, metabolic disturbance, or endocrine dysfunction." Their studies tend to prove that trauma certainly has a definite effect on the production and continuance of cartilage degeneration. Key<sup>3</sup> notes that several types of reaction in cartilage may result from the same type of injury, and calls attention to the

fact that in his experimental work, "if two joints be subjected to practically identical operative procedures one may return to a practically normal condition and the defect may be healed by cartilage which approaches the normal articular cartilage and there may be no reaction in the bone or joint except the deposition of a very small amount of subperiosteal bone on the sides of the joint, while in the other joint a condition resembling severe hypertrophic arthritis may develop. In some cases animals developed a rather marked degree of arthritis in one knee, while the other knee which had been subjected to a practically identical operative procedure developed almost no arthritis at all."

Our own experimental work, performed by Dr. O. H. Horrall and myself, to be reported at a later date, did show, however, a few constant characteristics of cartilage injury and healing. These are mentioned briefly here because the reactions correspond very closely to the pathological conditions found in various joints at the operating table in certain types of arthritis, which we considered due primarily to trauma, or trauma plus infection or toxemia which, added into a total, means the wear and tear of life. The trauma is often found in disarrangement, overweight, or primary injury, and these in some cases may be the sole cause.

From the Division of Surgery, Northwestern University Medical School and Passavant Memorial Hospital.

<sup>1</sup>Magnuson, P. B. Protein arthritis. *J. Bone & Joint Surg.* 1936 8: 839-844.

<sup>2</sup>Bauer and Bennett. Experimental and pathological studies in the degenerative type of arthritis. *J. Bone & Joint Surg.* 1936 18: 1-18.

<sup>3</sup>Key, J. Albert. Experimental arthritis, the changes in joints produced by creating defects in the articular cartilage. *Bone & Joint Surg.* 1930 29: 725-739.

We have opened and inspected a total of 83 joints in 72 patients suffering from various forms of arthritis and it is from the experience gained in this series that this report is made. We consider in this paper however only one phase of the surgery of arthritis and that is the reaction of cartilage in so called degenerative arthritis and what may be accomplished by the removal of what in our opinion is one of the major causes of prolongation of symptoms and disability in these patients. *In my opinion often repeated small trauma is the major cause in this form of arthritis and this is based on our experimental work and the observation of joints at the operating table.*

The spectacular results that have been obtained by removal of rough and irritating material indicates that after the roughness has started it automatically continues and becomes progressively worse as a result of this constantly increasing trauma caused by motion and weight bearing.

In our experiments performed on dogs there were certain consistent reactions to trauma of cartilage which were very definite. First cartilage which has been cut or broken away from its surroundings has no tendency to heal in from the sides as do epithelial surfaces (Fig. 1). Therefore it would seem that cartilage once fractured would leave a permanent defect and rough spot. A cork borer driven through the cartilage and underlying bone and a plug of bone and cartilage being removed the underlying bone curetted out and the plug countersunk below the level of the surrounding normal cartilage the bone will heal entirely and be revascularized while the defect will be obliterated completely in the course of 90 to 120 days. However the outline of the cartilage defect will remain. Although the cartilage which is countersunk below the level of the surrounding areas may build up to the level of the surrounding surface and be thicker from matrix to surface than the surrounding cartilage the defect made by the cut through the cartilage cells will not heal laterally and remains indefinitely as a cut or fissure (Fig. 2).

The growth of cartilage takes place in straight columns from the matrix toward the surface not laterally as does epithelium. If

hyaline cartilage be stripped up from the surface parallel with the matrix within a few weeks its character has changed from hyaline cartilage to fibrocartilage which acts as stringy bands between the joint surfaces and consequently it becomes a mechanical irritant. If the cartilage has been traumatized beneath this area there is condensation of cartilage cells and nuclei which stain poorly. The columnar appearance of the cartilage cells disappears and eventually this surface becomes rough and granular and continues the irritation of the joint on motion because of the degenerated rough substance within the joint.

If an incision is made perpendicularly through the cartilage into the bone and then beneath the surface of the cartilage a Y cut is brought out practically parallel to the matrix so that the outer surface of the cartilage is cut off from the matrix lying beneath (Fig. 4) the cartilage cells distal to this horizontal incision show condensation of nuclei with poor staining as far back as the cut extends and the area ultimately degenerates into fibrocartilage and everts into the joint forming a rough area. This same degeneration is seen whenever there is interference with the nourishment of cartilage cells and occurs regularly and consistently if the matrix is damaged or its source of supply is cut off. However if the cartilage is completely gouged out including the matrix and into the underlying bone leaving a cup shaped area there is no tendency toward regeneration. The defect is filled in somewhat by fibrous tissue the margins of cartilage on each side of the defect if not injured will retain their normal hyaline character but if injured will degenerate into fibrocartilage or fibrous tissue and form rough areas around the margin of the defect (Fig. 5). The gouged out area does not act as an irritant apparently because the cartilage on the opposing surface of the joint seems to give no evidence of irritation but where the opposing surface comes in contact with the rough areas along the edge of the defect there is roughening of the cartilage and gradual degeneration.

The production of these injuries to cartilage however did not result in the occurrence of typical findings of degenerative arthritis. There was no building up of perioosteal bone



Fig 1

around the edges of the joints. The reaction was confined entirely to the cartilage and was apparently local.

Many other experiments were tried to produce the joint pathology so often seen in the human. These included the injection of irritating chemicals, injection of bacterial toxins, severe trauma to cartilage over a wide surface of the joint, and the introduction of foreign bodies. So far as we were able to determine all these things were irritating factors and produced in some cases pain or joint irritation, but did not produce proliferation of bone and broader degeneration of cartilage in areas other than those immediately involved. We were able to produce the typical picture of degenerative arthritis in only one way, and that was by allowing the animal to subject the joint to often-repeated slight trauma. This was done by cutting away the medial and



Fig 3

crucial ligaments of the knee and allowing the animal free range of exercise. Those dogs, which were kept in the confinement of the ordinary cage, did not show proliferation of bone or degeneration of cartilage in the experimental joint. It was only by permitting free exercise in ample space which allowed the unstable joint to sustain cross strain constantly, that the exostoses around the edge of the joint appeared. In animals so treated there was deposition of subperiosteal bone around the edge of the joint, which began to appear in about 3 months and in from 6 to 9 months produced typical exostoses such as are seen in hypertrophic or degenerative types of arthritis. These exostoses appeared before any considerable amount of degeneration of cartilage was observed on the surface of the joint, even



Fig 2



Fig 4





Fig 5



Fig 6

on the weight bearing surfaces where one would naturally assume that most of the trauma occurred in walking and running (Fig 6)

The cause of the proliferation of bone around the edges of these joints which are constantly traumatized is unknown and has remained unexplained by all the authors on this subject and is still unexplained so far as I am concerned. It would seem to be an effort to throw up an abutment and limit the motion of the joint because it occurs most frequently on the lateral margin which would have a tendency to widen and flatten the joint in order to produce more stability. It is the blocking and irritation of the joint caused by these exostoses that in the human not infrequently makes it impossible to extend the joint fully and in my opinion this is one of the causes of prolonging and aggravating the already existing symptoms. When motion of the joint is limited the patient continues to make it function as much as possible in an abnormal position which throws further cross strain on the joint and continues the pain and aggravates the disability purely by mechanical irritation.

It was on this theory that the procedure to be described was developed. There have been 83 patients operated on for various types of arthritis, 62 of whom have had the degenerative or hypertrophic form of arthritis. Sixty of the 62 have made a complete recovery from their symptoms. In this report there are considered only cases of the degenerative form which has been commonly called hypertrophic arthritis. It is difficult to say which of them had contributing cause. In 7 cases infections were found and eliminated prior to

operation. In 4 there was evidence of chemical or metabolic disturbance and in 31 there were no findings except those locally in the joint. In all cases operation was performed because other forms of treatment did not give relief—heat, counterirritation, rest with traction, stimulation of metabolism, change in diet and the like had all been tried. Therefore with the idea that the mechanical roughness of the joint was the primary factor in continuance of the symptoms and disability, operation was performed. We believed that the roughness within the joint was responsible for the gradual building up of joint obstruction in the form of rough surfaces and exostoses around the margin and that the synovial membrane was not in any way responsible for the symptoms or the continuance of the symptoms.

The pathological process found in the case which were proved to have possible infectious or toxic conditions did not differ from that found in those which were believed to be

I have seen which related as usual in the past with the operation. The results of the operation are being followed up and the results of the operation are being followed up and the results of the operation are being followed up.





Fig 4 Cefar



Fig 3 Spec n ft mt th t



Fig 5 Cefar



Fig 18 Case of Mrs R left knee



Fig 20 Case of Mrs R, left knee



Fig 17 Case of Mrs R left knee

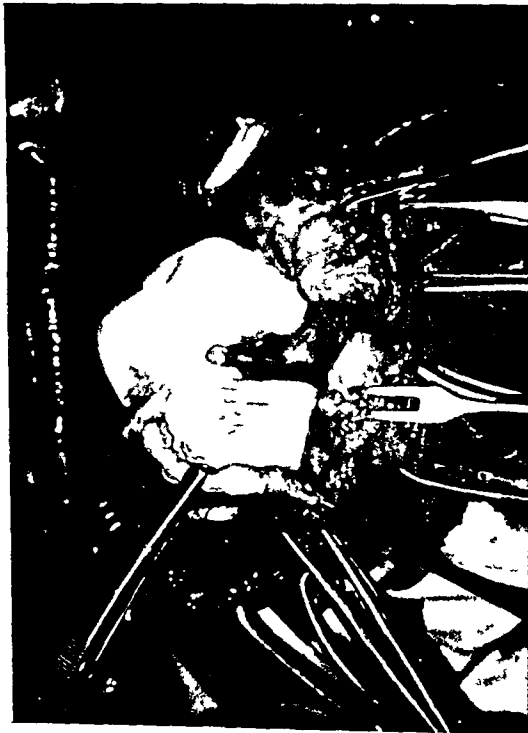


Fig 19 Case of Mrs R, left knee

*Joint Débridement—Surgical Treatment of Degenerative Arthritis —Paul B. Magnuson*

(Photography by Clarence B. Mitchell)





Fig 7

purely traumatic in origin. In 12 cases the procedure to be described has been done on two corresponding joints in the same patient, and in this group the joints have remained free from symptoms to this date. At this date the time since operation varies from 16 years to 6 months, which would indicate that the symptoms do not return after the removal of what is believed to be the aggravating cause, namely, roughness within the joint.

There are two forms of degenerative change encountered. One is a surface roughening of hyaline cartilage (Fig 7) beneath which, in the earlier stages, is found normal hyaline cartilage. This degeneration starts apparently from the surface and progresses toward the matrix. In the earlier stages this rough surface can be removed, leaving a layer of normal hyaline cartilage covering the ends of the bone. The defect will be filled by growth of the cartilage cells and a smooth normal joint will remain. The regeneration of normal cartilage depends upon the integrity of the matrix and the viability of the cells underlying the degenerated area. If the whole thickness of cartilage has not been involved one may expect to restore practically a normal joint. If the degeneration has progressed down to the matrix, the

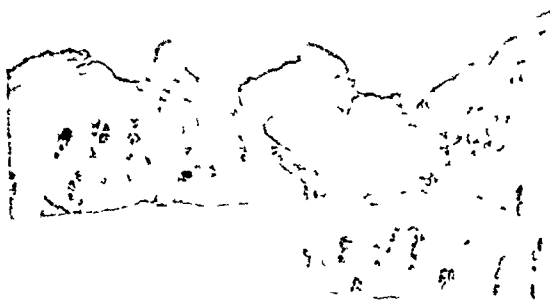


Fig 8

surface of the joint will be covered by fibrocartilage after the degenerated hyaline cartilage has been removed, but this seems to serve as quite a useful friction-preventing covering for the underlying bone, much as does the fibrous tissue which forms around the ends of old ununited fragments in a fracture.

Another type of degeneration apparently starts at the matrix and works in the opposite direction. On the surface of an apparently normal area there will be seen a little blister, sometimes so insignificant that unless the light falls obliquely the eye will not catch it, although the moist gloved finger may feel a slight elevation of the surface (Fig 9). If a horizontal slice is removed from the surface, including this blister at about the center, there will be found beneath the surface a degenerated area (Fig 10) with normal hyaline cartilage surrounding it. Usually there is a little discoloration at one side with indication of a fissure or breakdown of cartilage like the handle of a dipper extending from the end. This area, when sectioned for microscopic examination, shows small, poorly-staining, irregular layers of hyaline cartilage with condensation of nuclei, fibrous tissue irregularly interspaced, and a mucoid material filling some of the spaces (Fig 8). In the same joint other areas are found which are apparently a continuation and advancement of the same process. Fissures are seen in the surface of the joint surrounded by irregular, roughened, mottled and loose cartilage. Stringy fibrous degeneration with yellowish discoloration is noted in some areas, with tendrils of fibrous tissue attached at their base to the degenerated cartilage, and these areas are surrounded by

perfectly normal hyaline cartilage the degeneration near the rough area gradually fading into normal hyaline cells (Fig 11) The handle of a scalpel may be dropped into a fissure in the center of this degenerated area and it will be noted that the edges overhang and the degeneration widens as it approaches the matrix being somewhat pyramidal in shape Underlying the fissure no normal cartilage cells are found The fissure extends completely through to the bone (Fig 12)

The cause or causes of these two types of degeneration are unknown Further experimental work is in progress in an effort to determine the causative factors Apparently when either type progresses to a sufficient degree the entire joint becomes eroded and the finale is the same in both types although progress is most rapid on the weight bearing surfaces At least in the earlier stages it is practically always confined to weight bearing or most frequently traumatized surfaces in the elbow the upper end of the ulna the olecranon in the hip the upper end of the femur the head in the knee the lower end of the femur and in the ankle the lower end of the tibia The greatest degeneration is noted over the areas which receive the greatest trauma in performing the function of the joint If there is disalignment of the joint as a result of fracture or faulty growth the degenerated areas are most frequently found on the side of the joint where the greatest pressure occurs (Fig 13) In this series of cases there are 11 hips 8 elbows 41 knees and 2 ankles

*The hip* I am at a loss to explain why the greatest degeneration occurs at the head of the femur on the weight bearing surface instead of within the acetabulum but uniformly we have found the cartilage much more roughened and degenerated on the head of the femur than in the acetabulum The exostoses appear around the head and extend down into the neck Exostoses develop all around the acetabulum as the condition progresses and the acetabular lip in some cases becomes calcified deepening the socket and taking a firm grip of the usually broadened head which limits abduction rotation and extension In these cases will be found an adduction flexion deformity which is more or less fixed The

exostoses around the head usually extend down onto the neck and thicken it and in the x ray film it gives the appearance of a shortened neck This type is found frequently in Perthes disease which has been arrested in youth or in slipped epiphysis which has healed and borne weight for a number of years The thorough removal of the overhanging acetabular lip and the removal of the edges of the broadened head and the exostoses extending down onto the neck will allow the leg to be brought into abduction At the time of operation the head can be rotated out of the acetabulum sufficiently by adduction and internal and external rotation to remove the roughened cartilage of the weight bearing surface Occasionally small foreign bodies will be found either free or attached to a pedicle lying along the edge of the joint which are sucked into the joint on certain movements and give acute pain and locking as they do in any other joint Although we have found these bodies in three hips there was no evidence of them in the x ray films which were of good diagnostic quality The x ray films were examined subsequent to operation when it was known where the foreign bodies were located and even then they could not be seen

*The elbow* In the elbow the mechanics of weight bearing are reversed and except in pugilists who traumatize their elbows severely in their occupation we have found most of the degeneration on the articular surface of the ulna particularly around the proximal two thirds of the joint surface of the olecranon with exostoses around the posterior edges of the lower end of the humerus where it comes in contact with the olecranon

In the exposure of the elbow it has been found that cutting the olecranon off well down toward the joint directing the chisel toward the lower and somewhat anterior surface of the humerus which removes the upper end of the ulna completely so that it can be reflected backward and upward gives the best exposure If the anterior two third or three fourths of the ulnar articulation is left in contact with the lower end of the humerus it is difficult to inspect the lower end of this bone far enough anteriorly to be sure the exostoses and joint surfaces are properly

cleared off. The olecranon, therefore, has attached to it about 50 per cent of the articulating surface of the upper end of the ulna, and when it is replaced it fits around anteriorly, serving as a grip on the lower end of the humerus, and this fragment of the upper end of the ulna is not as easily displaced as when the olecranon is taken off as such. In one patient, an enthusiastic bowler, the cartilage had entirely degenerated in a strip completely across the olecranon from side to side, and there was a fine sharp edge along both sides of the olecranon, extending down to the ulna, which was actually sawing the synovial membrane. The patient had intermittent swelling and locking of the joint, not acutely as in a foreign body, but coming on over a period of an hour or so after the attack occurred. Blood was found in the joint and the synovial membrane was lacerated on both sides. The patient made a complete recovery after the removal of the rough cartilage and the sharp edges along the sides of the olecranon.

*The knee* Inasmuch as knees have been the joints most frequently affected, the operative procedure is described in detail. It has been our experience that if this procedure is carried out in other joints the results will be the same, provided the cases are carefully selected.

A medial parapatellar incision is made from the medial edge of the attachment of the patellar tendon at the tibia to about 3 inches above the patella, the medial half of the quadriceps being cut from its patellar attachment and split longitudinally. The patella is retracted laterally as the knee is flexed, thus exposing the entire anterior and inferior surface of the lower end of the femur and part of the upper surface of the tibia. The joint surfaces are well exposed, as is the articular surface of the patella (Fig 14). A sharp, thin bladed chisel is used to remove the exostoses from both condyles with the edge of the synovial membrane attached. In some cases the synovial membrane is slightly overhanging but not adherent to the joint surfaces, as is found in the atrophic form of arthritis. The cartilage on the condyles is then shaved. Care must be taken not to leave any transverse ridges such as shown in Figure 15. If ridges are left they should be longitudinal so they

will act as tracks on which the opposite side of the joint can glide, and not as obstructions in the plane of motion. All degenerated cartilage is removed down to bare bone. In old cases the patella is found to be widened, the cartilage very thin, yellowish and granular on both the lower end of the femur and the articular surface of the patella. The patella must be narrowed so that it will slide between the condyles without obstruction, and a comparison of Figures 15 and 16 will show the amount of narrowing, sometimes as much as 50 per cent, that will make a useful joint. In this illustration the patella is cut off square to emphasize the amount of lateral margin remaining. These sharp corners, of course, are removed before the joint is closed, as are also the sharp edges which in themselves would act as irritants (Fig 16).

The fibrous degeneration is seen most plainly in the earlier stages of the disease (Fig 17). This fibrous degeneration is completely cut away, leaving all the healthy cartilage possible, but allowing no rough surfaces to come in contact (Fig 18). In the earlier stages the joint margins are not found to be inflamed as they may be in the later stages. They are covered with thin fibrocartilage and hyaline cartilage, and have a pinkish blush without the extremely engorged appearance of the later cases (Fig 19).

The upper end of the tibia is explored and if any rough cartilage exists it is removed. The menisci are examined and removed if they are degenerated. This has not been found in most instances, but in three joints rather sharp exostoses were found extending from the upper end of the tibia, which protruded upward and impinged against the condyles of the femur when the knee came into full extension (Fig 20).

When all roughness has been removed from the surface of the condyles, the margins of the condyles and the articular surface of the patella and upper end of the tibia, the operation is complete, and not until that time is it complete. The success of the procedure depends on the complete removal of all mechanical irritants from the joints. No halfway procedure will give a satisfactory result, in my experience.



The synovia is sutured plain No catgut interrupted sutures being used. The ligament is sutured in the same manner and the skin with continuous dermal sutures. Pressure dressings are applied two laparotomy pads on the flexor surface and two on the extensor surface with a non rubber elastic bandage applied snugly over them. This is reinforced by another laparotomy pad over the same area and a firm gauze bandage over all. Buck's extension below the knee to which 6 to 8 pound of weight is applied when the patient is returned to bed sometimes adds to his comfort for the first few days. The first compression is removed in 36 hours the second in 72 hours and comparatively little swelling is found within the joint.

In operation on other joints similar compression is used put on in a way to maintain strong pressure without interfering with circulation.

#### AFTER TREATMENT

Motion is started on the fourth day. Muscle exercise is of prime importance. The patient should be required to use the muscles both in flexion and extension and it has been found helpful to synchronize the use of the muscles on both extremities moving the unaffected limb at the same time that effort is made to move the affected one. This must be done regularly and consistently. Asisted motion is very low and steady. In the knee it has been our custom to build the flexion up by inserting laparotomy pad one at a time between the mattress and the flexor surface of the joint up to 45 degrees during the first week after motion is started gradually increasing each day. Pads are inserted for one hour and removed during the next always one at a time.

If it is a weight bearing joint the patient is put on his feet on the eighth to tenth day following operation. Prior to this it should be possible for the patient to completely straighten the knee or hip. Too much importance cannot be attached to this point. No pain is caused if the weight falls in the right line but if there is slight flexion of the joint the soft tissues surrounding the joint which are painful and tender will be strained the patient will have acute pain and will not

rest weight on the joint because of fear of pain once it has occurred. It has been my custom to assist the patient out of bed and while he is sitting on the edge of the bed or leaning against it get the joints in proper weight bearing line. I then stand behind the patient supporting the elbows and forearms on my arms and forearms. The patient is requested to hold his chest up tail in knees back and hips straight. It is easier to do this standing behind the patient supporting him strongly than to stand in front of him or allow him to use crutches under which circumstances he always has a tendency to bend forward. If the patient is straight his joints are in proper weight bearing line and he will not have pain.

The first day's lesson is in standing only. He is assisted into bed without causing pain. On the second day in the same position and with the same support he is encouraged to take two or three steps the surgeon being sure that the patient does not lean forward as he would were he using crutches or being supported from in front. He walks with the knees stiff and the hips stiff until he finds he can bear weight confidently and then each day with trained assistants or preferably the surgeon himself acting as support and instructor the patient begins to walk. He is never allowed to limp moves one foot forward evenly with the other. The assistant stands back of him supporting his weight and insisting that the body move forward smoothly and evenly as in normal walking. These patients are never given crutches but are allowed to use two canes with the upper end of the cane and the hand held firmly against the thigh chest up hip straight knees back tail in. The lessons are given each day until the patient has confidence that he can bear weight and he will have no pain when he does bear weight.

It is a good plan before the patient begins the walking exercises to have asisted motion while in bed. In the case of the knee the patient may sit on the side of the bed with the leg hanging over the side the heel supported in the palm of the surgeon's hand and be instructed carefully in muscle contraction and relaxation so that he may see the knee move under his own power and see the muscles

work. In the case of the hip, a sling is put under the knee and a rope attached to this sling is run up over a pulley on a frame and terminates in a handle which the patient can grasp and give himself assisted motion. It is important that the hip and knee come into full extension after each flexion, and they will not do this if they are simply allowed to come in contact with the mattress, the body sinks into the mattress at the hip level, consequently there is slight flexion of the hip and, as a result, slight flexion of the knee. Therefore it is necessary to turn the patient into a prone position several times a day and see that the affected weight-bearing joint comes into full extension.

Gentle rhythmic massage is given daily, as is also muscle training. Heat is helpful in any form chosen, and for a substantial part of every 24 hours. No force is used at any time on these joints. If these procedures are carefully followed, it is perfectly astonishing how soon the patient will have 90 degrees of motion and full power in the joint. Too much emphasis cannot be put on careful supervision of after-treatment.

#### SUMMARY

Degenerative arthritis is probably the result of often repeated small trauma. It may be aggravated by low-grade infection or chemical and metabolic toxemia. Once roughening in the joints is established, the mechanical irritation of this roughening is sufficient cause for prolongation of symptoms and disability.

Degenerative arthritis is a disease of the latter part of three score years and ten, and has been said to be the result of the wear and tear of life. In my opinion this is true, but we have not given sufficient consideration to the factors which cause the wear and tear, which should be eliminated if possible before surgical treatment is instituted.

Thorough removal of all mechanical irritating products of joint degeneration will, in a large percentage of cases, render the patient symptom free. Even when the degenerative process has progressed to a point at which there is practically no healthy cartilage, the operative procedure described herein will result in remarkably good joint function. The denuded areas are covered with fibrocartilage which serves as a satisfactory substitute for hyaline cartilage in the advanced cases, and in the less advanced cases the progress of the disease is stopped, or at least long delayed, by the removal of mechanical irritants.

Removal of the synovia has not been found necessary and has been done only in some cases of atrophic arthritis which are not reported in this paper.

The selection of patients and the after-treatment are as important as the operation itself. If the patient is not willing to help, the operation had better be left undone.

The picture of hypertrophic or degenerative arthritis as seen at the operating table in various stages of development is synonymous with the findings produced in animals by often-repeated small trauma of an unstable or constantly traumatized joint.

# EFFECT OF STORED CITRATED BLOOD TRANSFUSIONS UPON PATIENTS WITH HYPOPROTHROMBINEMIA

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CITRATED stored blood for transfusions is useful when given to patients with a hypoprothrombinemia. In certain instances a marked improvement in the plasma prothrombin level may be reached. However, since the introduction of synthetic compound with vitamin K, a activity which have been used to correct an existent hypoprothrombinemia in patients it has not been necessary to depend upon blood transfusions to improve the plasma prothrombin level to combat any tendency toward bleeding.

A number of reports have been published concerning the prothrombin content of stored citrated blood. Lord and Lastore reported that the prothrombin content of stored blood was relatively little diminished. They used the method of Warner, Brinkhous, and Smith for their determinations of prothrombin clotting time. However, Rhoad and Panzer, using a modified Quick method, found that the prothrombin content of stored citrated blood rapidly decreased so that by the seventh day of storage the blood was of little value for its prothrombin content. Ziegler, Osterberg, and Hovig also studied the prothrombin content of stored blood and found that the decrease in the prothrombin content was gradual and not as rapid as that found by Rhoads and Panzer. They concluded that old blood was not suitable for raising the plasma prothrombin by transfusion. However, no specific optimum time was given. Their specimens were studied over a period of 36 days, which is much longer than one preserves citrated blood for transfusion.<sup>1</sup> Usually, blood older than 10 days is considered not desirable for transfusion. They found that after 12 days of storage the prothrombin varied from 60 to 80

per cent of its original amount. Quick studied preserved blood and concluded that the prothrombin diminishes rapidly within 24 hours. He supported the conclusion of Rhoad and Panzer in that stored blood was inferior to fresh blood for controlling bleeding in jaundice. Reinhold, Valentine, and Ferguson studied the effect of storage on the prothrombin content of citrated blood and found that the level gradually decreased, thus supporting the original contention. They defended the use of stored blood as transfusions for prothrombin deficiency but proposed the facts that the relative amount of prothrombin in 500 cubic centimeters of blood compared to the total in the body was small. Thus any transfusion, even if it were fresh, would raise the prothrombin level only slightly. However, the value of transfusion in patients with bleeding should not be underestimated.

The literature contains no clinical evidence to prove or disprove the value of stored citrated blood as a source of prothrombin for patients with a hypoprothrombinemia. Thus patients with low plasma prothrombin level were given transfusions of blood varying in age and the effect was noted.

## PROTHROMBIN CONTENT OF STORED CITRATED BLOOD

Seventeen specimens of stored citrated blood were studied over a period of 10 days for their prothrombin content.<sup>2</sup> The prothrombin time for the donor and the specimen of blood immediately after citration was found to be the same in every instance. The plasma prothrombin levels for each specimen were recorded daily (Chart 1) by the tenth day of storage (the plasma prothrombin level in

F m th D pa time t Surg ry C sity f Ill s C  
f g f Med ine nd Cook Co y ff p cal  
Blood t r al is t sed ier day f t ag t  
th Cook Co y ff p cal

M bod i d t ma t f th plasma thr mb sel  
th sm th t f h ul w ex d d pe t g t  
mal p ma p thr mb t m Th pec an w ed d  
r f f d th a o d t d with th sam p por  
t f c t t sed pr par t f blood f t f s u  
b C k Cou ty j p t l blood ba k

the 17 specimens studied averaged 54 per cent of the normal level

#### EFFECT OF THE INTRAVENOUS INJECTION OF SODIUM CITRATE UPON NORMAL PLASMA PROTHROMBIN LEVELS

Six patients were given 70 cubic centimeters of 2.5 per cent solution of sodium citrate<sup>1</sup> intravenously and the effect was noted upon the normal plasma prothrombin level. After the administration of the citrate, 4 patients showed no immediate change in the plasma prothrombin (Table I). One patient in this group had a slight drop in the level after 36 hours. Patient E Mc had an immediate drop which returned to normal within 12 hours. One patient, F C, had a slight rise. Recovery was rapid and no ill effects were noted in any of the patients studied. It was concluded that any effects on the prothrombin clotting time which occurred after transfusion with citrated blood were not due to the citrate used.

#### EFFECT OF CITRATED STORED BLOOD UPON PATIENTS WITH A HYPOPROTHROMBINEMIA (TABLE II)

One patient received a blood transfusion of blood which had been stored for 1 day. Before the transfusion the plasma prothrombin level was 66 per cent, immediately after the transfusion it was 70 per cent. In 12 and 24 hours the level was 100 per cent. After 36 hours it dropped to 79 per cent. The effect noted was good.

Six patients received transfusions of 2 day old blood. Two patients, W McK and E G, showed a definite rise in the plasma prothrombin. One patient, J F, had an immediate drop which returned to the initial level within 12 hours. Another patient, B P, showed a drop which remained until 36 hours after transfusion, when there was a rise above the initial level. Patient P S showed no change until after 36 hours when the level reached normal. Since the patient was improving from her disease, we considered the rise as due to the patient's improvement and not affected by the transfusion. Patient A R, showed no change after the transfusion. No harmful

<sup>1</sup>This amount of sodium citrate is used for anticoagulation of 500 cubic centimeters of blood.

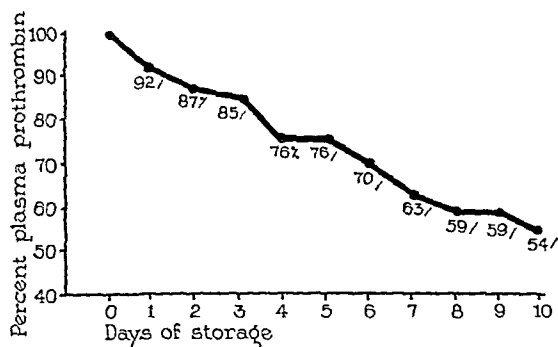


Chart 1. The gradual drop in the percentage of plasma prothrombin in 17 specimens studied. The percentage recorded for each day of storage is average for 17 specimens.

effects were noted, and in some instances an improvement in the plasma prothrombin levels was found.

Three patients were given 4 day old citrated blood. In all patients there appeared to be no immediate effect on the plasma prothrombin. In 2 patients, G I and C B, the level dropped after 12 hours. These patients recovered their initial level in 24 hours. Patient R G reached 100 per cent in 24 hours.

Four patients received 5 day old blood. Patient A M reached a normal prothrombin level immediately after the transfusion. This was maintained for 12 hours. Patient W P reached a normal in 12 hours. D W had a slight drop and then reached normal in 24 hours. Patient A K had a slight rise. The effect in these cases was much better than expected. No harmful effects were noted in these patients.

TABLE I—EFFECT OF INTRAVENOUS ADMINISTRATION OF CITRATE<sup>\*</sup> UPON NORMAL INDIVIDUALS

Patient	Per cent plasma prothrombin				
	Before citrate	Immediately after	12 hrs after	24 hrs after	36 hrs after
C S	100	100	90	95	100
C M	100	100	100		
A J	91	92	96		85
E Mc	92	79	92		
W K.	100	100	100	100	100
F C	90	95	83	91	

\*70 c cm of 2.5 per cent solution

TABLE II—EFFECT OF CITRATED STORED BLOOD ON PLASMA PROTHROMBIN LEVEL IN PATIENTS WITH A HYPOPROTHROMBINEMIA

Day	Patient	Diagnosis	Prothrombin %				
			Before transfusion	Immediately	1 hr	4 hr	36 hrs
1	J.B.	Cholecystitis	66	7	00	00	7
	W.M.K.	Carcinoma of the bladder	34	5		56	43
	E.G.	Carcinoma of stomach	6	4	7	46	
	J.F.	Cholelithiasis	7	55	73	60	
	A.R.	Cholecystitis	69	7	69	7	
	E.P.	Cholelithiasis	7	59	8	6	83
	P.S.	Cataract of eye	69	6	63	66	00
	R.G.	Cholelithiasis	78	7		00	89
	G.I.	Cholelithiasis	80	79	66	75	80
	C.E.	Cirrhosis of liver	5	56		53	5
5	W.P.	Cataract of eye	53	62	00	67	
	A.K.	Carcinoma of pancreas	4	34	5	55	
	A.M.	Cholelithiasis	5	00	00		
	D.V.	Carcinoma of prostate	60	5	88	00	
6	J.H.	Cholelithiasis	26		7		
	W.M.	Cholelithiasis	6	3	69		8
9	M.B.	Cholelithiasis	5		67		
5	M.B.	Cholelithiasis	55		7		
	S.V.	Cholelithiasis	59	78	55		
11 months	K.S.V.	Cholelithiasis	5		82		

## OBSERVATIONS

Two patients were given 6 day old stored blood and in both instances there was an immediate rise in the plasma prothrombin level. After 12 hours there was a drop to the former level.

One patient received a transfusion of 9 day old blood and showed a definite improvement after 12 hours. When the level dropped after 24 hours to 53 per cent a transfusion of 5 day old blood was given and again an improvement was noted.

One patient was given a transfusion with 10 day old blood and an immediate rise was noted. In 1 hour the level again dropped. At this time a compound with vitamin K activity ( $\alpha$ -methyl-1,4-naphthoquinone) 1 milligram 3 times a day was given orally. The level before starting was 57 per cent. Twelve hours after the vitamin K compound it rose to 83 per cent. The value of the synthetic compound in these conditions is noteworthy.

Prior to the discovery of vitamin K blood transfusions were used to combat the tendency to bleed in patients with obstructive jaundice. Judd used the procedure before operation in these patients and found that the tendency to bleed after operation decreased. The mechanism of this action was not known.

Patients with jaundice of an obstructive nature are now often found to have a hypoprothrombinemia which predisposes them to bleeding. Such conditions may be corrected by giving these patients vitamin K compounds. Therefore it would not be necessary to depend upon blood transfusions. This does not signify that one should disregard the value of transfusions before and after operation.

The amount of prothrombin in 500 cubic centimeters of blood is small compared to the total prothrombin content of blood in the body. The prothrombin as determined by

the Smith test, is equal in the donor and in his citrated blood sample immediately after being drawn. Stored citrated blood gradually loses its prothrombin content during storage. A transfusion with this blood would increase the total content of the body's prothrombin only slightly, thus, it theoretically should have little value in the treatment of hypoprothrombinemia. On the contrary in several instances there was a marked improvement in the plasma prothrombin level even after 10 days of storage when the prothrombin content averaged 54 per cent of its normal value. Such an effect of the blood transfusion upon the prothrombin level was often greater than could be accounted for by the prothrombin contained in the transfused blood. Such an effect may be explained upon the basis of added vitamin K present in the transfused blood. An investigation is now being made to determine the vitamin K content of stored citrated blood. One could also assume that there was a stimulating or catalyzing effect induced by the transfused blood. The age of the blood apparently makes no difference as to the effect obtained. Thus one may state that stored citrated blood transfusions are useful in elevating the plasma prothrombin and may be used up to the tenth day of storage without harmful effects upon the plasma prothrombin level.

#### SUMMARY

When citrated stored blood is given to patients with a hypoprothrombinemia, it is effective in elevating the plasma prothrombin and may be used for transfusions up to the tenth day of storage with beneficial effects upon the plasma prothrombin level. However, because of more rapid and effective action, compounds with vitamin K activity

should be used preferably to correct the existent hypoprothrombinemia, citrated stored blood should be used as an adjunct in the treatment of the primary disease rather than for its effect on the prothrombin level.

The effect of a blood transfusion upon the prothrombin level is often greater than can be accounted for by the prothrombin contained in the transfused blood. Such an effect may be explained on the assumption that vitamin K is present in the transfused blood or on the assumption that a stimulating or catalyzing effect on prothrombin formation has been produced.

Citrated stored blood gradually loses its prothrombin content, in a series of 17 cases the average content by the tenth day of storage was 54 per cent of normal. However, the elevation of plasma prothrombin in patients given a transfusion was approximately the same regardless of the age of the blood and its prothrombin content.

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# THE BASIS OF THE HISTOLOGICAL DIAGNOSIS OF CARCINOMA

With Special Reference to Carcinoma of the Cervix and Similar Lesions

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THE clinical diagnosis of cervical cancer is often indefinite and demands histological control. This truth is evidenced by a study of 5000 curettage and biopsy specimens. In 774 or 15 per cent of these specimens the clinical and histological diagnoses were in disagreement. Of these 270 were cervical biopsies and in 20 a definite clinical diagnosis was found to be in error. In 250 other cases biopsies were taken because of clinically suspicious lesions of the cervix but only 36 of these could be verified histologically as cancer. Without histological control 194 of these patients would have been left without a basis for therapy.

The question naturally arises as to whether the histological diagnosis is in reality more trustworthy than that obtained by clinical means. Actually this question has often been raised since the beginning of the use of histological diagnosis 60 years ago. At that time Ruge and Veit in Berlin held that histological methods offered the only acceptable criteria for the diagnosis of cancer particularly of the endometrium and cervix. These authorities pointed out that considerable experience is required in the evaluation of material obtained by curettage and cervical biopsy. The poor results of surgical therapy to tumors of these tissues might be much improved if histological methods were used to allow recognition of the diseases in the early stages of their development. It is now of course generally agreed that Ruge and Veit were correct in their demand that histological investigation be considered an essential part of the diagnosis of tumors in this region. It is hard for us to realize today that these men had to

carry on a long struggle against resistance even by outstanding gynecologists and pathologists. At the present time there is a general acceptance of this rule although there is still occasional doubt raised as to the finality of histological diagnosis. It is wise then to evaluate critically from time to time the fundamental features of a histological diagnosis of cancer.

It has been suggested that there are certain dangers in obtaining material for biopsy. It has been said that curettage and biopsy in cision can produce serious results when carcinoma is present. Not only it is said may infection be introduced but vessels may be opened to allow the entry of cancer cells with the resultant production of metastases. It is odd that this hypothesis has never been experimentally tested.

In order to reach a conclusion it would be necessary to examine large numbers of specimens from which biopsies had and had not been taken. With this in mind I have carefully investigated the region of the biopsy wound in breasts and uterus removed from 1 to 14 days after biopsy and have never been able to demonstrate any relation between tumor spread and the trauma incident to removal of material for histological examination. Even if such spread should occasionally occur it does not approach the danger of the large number of unnecessary therapeutic procedure which would be carried out in the absence of histological diagnosis. Paterson and colleagues published an important investigation of 166 cases of squamous cell carcinoma. In this investigation 99 cases in which patients were operated upon after excision for biopsy had a smaller percentage of metastases after several years than the cases with out biopsy.

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December 6, 1930. First lecture  
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The histological diagnosis of cancer must be made as accurate as possible. Problems will arise in arriving at both a positive and a negative diagnosis. In order to check on the biopsy diagnosis, careful examination should always be made of the material removed when surgical therapy is undertaken. It is possible that surgical damage to the tissue may occasionally make this an unreliable check. It is also possible that a very small tumor has been entirely removed by the biopsy procedure. This factor occurs very seldom and it is dangerous to use it to explain a failure to confirm the pre-operative diagnosis. In cases in which radiation therapy is the method of choice it is most often possible to obtain sufficient quantities of material to make the diagnosis certain before this form of therapy is undertaken.

When one has to deal with large numbers of specimens each year, failure to recognize histological malignancy will not long escape attention so that these diagnoses are automatically controlled. But the question continues to arise in regard to the finality of the histological diagnosis. This has been studied by means of an evaluation of the end-results in a large group of patients from whom material had been obtained by curettage or cervical biopsy, and examined from 2 to 5 years previously. The findings have been published in detail (8, 10). Particular attention was paid to those cases which showed excessive hyperplastic response in the endometrium in such conditions as cystic glandular hyperplasia, endometrial polyps, or squamous change of the endometrial epithelium and to those in whom erosion healing or polyps of the cervix showed excessive epithelial activity. Some of these were followed during 8 to 12 years after the original examination.

The results of this study have apparently justified the criteria used in the original diagnosis. The fact that no undiagnosed cancer has come to light in the series would seem to be fairly conclusive evidence. One should, however, always bear in mind the fact that there is no infallible judgment, and experience has only served to make one even more cautious. Thus, the careful study of both biopsy and operative specimens and the follow-up

control of patients have been the two methods used in the control of the histological diagnosis. The diagnostic criteria are, then, based upon clinical standards and not upon theoretical considerations. Histological examination is only one of the essential studies in this field, and it should be carried out in close co-operation with the clinic.

Following the stages of the historical development of our knowledge of the subject, one might well begin by asking these logical questions: What is the microscopic appearance of the tissue in clinical cancer? What tissue disturbances may be seen which differ from the normal or the benign alterations?

1 Changes occur in the epithelial cells which at first may deviate only slightly from the normal. (a) For abnormally long periods the cells may show evidence of the lack of the normal processes of ripening or maturity, (b) they often change their size and shape. This is particularly evident in the nucleus whose whole structure changes, (c) there is an increase in the nuclear chromatin, and (d) sometimes the whole character of the normal cell is changed.

2 The cancer cells continuously reproduce themselves so that the whole normal form of the tissue is lost. Occasionally, even when the cells and their nuclei are not essentially changed, the form of the tumor, as a result of continuous growth, is often sufficient for a diagnosis of malignancy.

This is best seen in adenocarcinoma in which, with comparatively little change in the individual cell, there are deviations from the normal gland form and multiple layering of the cells to produce thick masses of epithelium. This may then grow to be elevated above the normal surface to produce adenomatous or papillomatous tumors.

3 The tumor cells may directly invade the neighboring tissue and destroy it. They may make their way into vessels, may be transported as emboli and may settle and develop elsewhere in the body to produce metastases.

Cancer shows then (1) variations from normal in the cells and particularly in their nuclei, (2) changes in the gross form of the tissue, and (3) invasion of other tissues, of vessels, and the production of metastases.



The third characteristic that of invasion is the most important from a clinical point of view. It has been placed last in the list not only because it usually appears last in the course of the development of the disease but to express opposition to statements still appearing in the literature to the effect that in invasion of surrounding tissue is the only adequate criterion of malignancy. It is the most striking and historically the first of the characteristics to be recognized. But the other characteristics appear earlier and must be recognized. Under these circumstances there can be no advantage in waiting for the development of later stages. It is necessary to arrive at a diagnosis at the earliest possible moment in the natural history of the cancer process. Microscopic changes in the cells are the earliest which can be recognized and these can be accepted as trustworthy before invasion. Adenocarcinoma of the body of the uterus is diagnosed by every pathologist from curettings which consist only of superficial tissue. The changed tissue form and structure are sufficient without evidence of invasion.

It is widely believed that the pathologist using the 3 general criteria here outlined can arrive with ease at a differential diagnosis of malignancy. It must be pointed out that somewhat similar changes may on occasion occur in benign tissue. The grossest sign of malignancy, namely invasion of the surrounding tissue, may be seen in such benign lesions as adenomyosis. Sections from the cervix and the vagina are to be seen in which the original tissue may be replaced by the invasive growth of endometrium whose stroma melts away the muscle and connective tissue (7, 9, 11). This can even invade vessels and very occasionally produce emboli and metastases. Similar findings are known to occur in other benign tumors as for example those of the thyroid.

One must be careful of generalizations in histological interpretation. Similar changes can have an entirely different significance in different organs. Many illustrations could be used to demonstrate the fact that no generally applicable rules can be formulated or applied to the diagnosis of malignancy as a whole. There is no single characteristic which justifies a diagnosis of malignancy under all condi-

tions. This is true of the changes in the cell themselves of the gross form of the tissue and of invasion. Even the dissolution of other tissue by some form of proliferation invasion of vessels and production of metastases lend no certainty in every case to the diagnosis of malignancy. The opinion might seem justified that the histological diagnosis is clouded by too many pitfalls and uncertainties. In reality however this is not entirely true but it would seem wise to sound a warning in order that the difficulties concerned shall not be underestimated. In order to avoid error wide experience in histological diagnosis is necessary as indeed it is in any other diagnostic endeavor. This experience must take into account clinical information. Without this the art of histological diagnosis would be based upon a false theoretical premise.

In the field of gynecology there are two disturbances of squamous epithelium which are not always adequately differentiated. These are the benign and the malignant proliferation of the squamous epithelium of the cervix. They hold in common the characteristics of superficial growth and invasion of the glands. In the course of this invasion they both show displacement and replacement of the cervical epithelium and may fill the gland lumen. It is characteristic of the benign lesion erosion healing that having reached this stage its demands seem satisfied and proliferation ceases. It requires the gland for this type of invasion. In contradistinction to this the carcinoma continues its proliferative course breaking through the basement membrane of the gland to invade the underlying tissue. It does not require the gland for direct invasion but uses it on occasion as a matter of convenience.

The accompanying illustrations demonstrate the process of epithelialization of erosions and cervical polyps. The differential diagnosis in each case has been confirmed by prolonged observation.

The benign epithelialization represents the healing of a cervical erosion. An inflammatory infiltration most often spread from the cervical mucous membrane comes to lie beneath the squamous epithelium of the portio. The destructive effects of this progress toward the

surface until all layers are destroyed and the erosion is produced. The mucus-producing epithelium of the cervix or its glands grows over the defect and this represents the first stage of the erosion healing. As the inflammation subsides the squamous epithelium advances from the margin of the erosion. It grows by a proliferation of its basal cell layer between the connective tissue and the mucous epithelium and may similarly extend into the glands. The mucous epithelium is lifted off and dies. Finally, both in the glands and on the surface, basal cells differentiate into layers, lose their unripe character and may fill up the glands as well as cover the surface. This process of ripening may proceed slowly. The filling of the glands may take considerable time and mucous producing epithelium may persist during this process.

This process of epithelization may be distinguished from early carcinoma by a recognition of the normal character of the cells. Figure 1 shows a section from the cervix of a 51 year old female and demonstrates healing glandular erosion. There is epidermization of the glands, the mucous epithelial cells are higher, their nuclei darker than that of the surrounding squamous epithelium. These cells spread between the mucous epithelium and the connective tissue. In some of the smaller glands there is only a single row of squamous cells. As the squamous cells proliferate they become multilayered. The mucous cells are pushed away from the connective tissue and finally disappear, as shown in one of the glands at the base of the picture. The squamous epithelium cells, centrally located, are larger and sharper than their basal cell row. The gland still has a lumen. To the left is a solid cell mass resembling a cancrroid pearl. To the right of the same figure are 2 glands showing an earlier stage of epidermization. In some areas the mucous epithelium is still in its original position, immediately next to the connective tissue. However, the basal row of squamous epithelium is beginning to undermine the mucous epithelium. In the center of the figure the long tubule has several branches, not completely filled with squamous epithelium. The uppermost of these branches appears to be a solid, independent mass. All



Fig 1 Epidermization of glandular erosion. Excision biopsy.

areas of glands after epidermization is complete appear as solid masses, if cut tangentially, and must be cut in series to show that they are parts of glands. In some of these solid masses one can find remnants of mucous cells or mucus. I repeat these well known facts because even today occasional errors of diagnosis are made and because epidermization is often erroneously called metaplasia. This conception is fundamentally wrong and



Fig 2 Excision biopsy from the portio. Flat section through the basal cells of epidermized glands of an erosion healing.



Fig 3 Cervical polyp

is based on noncritical judgment of single slides instead of series or reconstruction. In erosion healing it is very often easy to show that the epidermization originates from the normal squamous epithelium on the periphery of the erosion. To understand the epidermization in the higher level of the cervical canal and also of polyps arising from this area it must be clearly understood that in some areas basal cells exist beneath the mucous epithelium. These cells have remained in this area since the early developmental stages as fetus and child at which time the entire cervical canal was covered with the squamous epithelium of the vagina. This was pointed out by the writer 30 years ago and confirmed by later work on the development of the vagina.<sup>1</sup>

During pregnancy the squamous epithelium of the vagina often covers the lateral areas of the cervical canal. Thus in adult life the basal cells of squamous epithelium can reach the upper part of the cervical canal and remain there. These basal cells are found under the mucous epithelium in apparently normal cervixes. A tangential or flat section can lead to confusion in diagnosis. Figure 2 is taken

from a clinically suspicious erosion of the portio in a 53 year old woman. On the left is the remainder of a gland lumen. In other sections all the solid appearing epithelial bodies presented lumina some of which could be followed to the surface. Some of the lumina contained only mucus others were lined by mucous epithelium. By chance many of the cervical glands in this section are cut tangentially showing only their basal cells. These cells are always more unripe than the inner layers and therefore appear darker. The diagnosis of benign erosion healing was made. No treatment was instituted and 3½ years later re-examination of the woman confirmed the prognosis.

One case such as this is not adequate proof but observation of large numbers of similar cases with various degrees of epidermization healing untreated by operation or radiation is decisive.

Polyps of the cervical mucosa are sometimes even more confusing. These are very seldom carcinomatous and even then many are secondarily invaded by carcinoma usually at the base. Since the polyps are often multilobular and wrinkled the very active epi-



Fig 4 Papillomatous leucoplakia following erosion healing. Invasion into a gland

dermization produces confusing pictures which quite frequently mislead investigators to diagnose carcinoma

Figure 3 shows a polyp of the cervical mucosa presenting a minor degree of epidermization. The first view (left above) is taken with low power, the details of the darker spots (*a, b, c, d*) are shown in the other pictures. In *d* the squamous epithelium is invading a gland, the mucous epithelium covers the reduced lumen. In *c* the squamous epithelium seems to precede the mucous epithelium along both sides of one gland, against its fundus and toward the surface. It is impossible to be sure of this without reconstruction of a series. In *b* the squamous epithelium lies partly on the surface and surrounds some of the smaller glands. In *a* the squamous epithelium undermines the mucous epithelium on the surface. The connective tissue is infiltrated by round cells. The epithelium throughout shows a moderate degree of ripening without atypical changes. It is apparent that the squamous epithelium arises independently in various areas.

There are some changes in the squamous epithelium as a result of proliferation which are easily recognized as benign (Fig 4). A degree of leucoplakia is seen in the epithelium of invading glands in parts of the area which had previously been an erosion. Papillomatous proliferation is benign, even when it seems to invade the connective tissue with very long projections of squamous epithelium,



Fig 5 Partly papillomatous leucoplakia of the portio of prolapsed uterus

as long as there is a clear basal row and normal layering (Fig 5). In these circumstances also, sections through the basal row may be deceiving.

Figure 6 shows a section from a wart-like proliferation of the squamous epithelium on the portio in a 20 year old virgin. The epithelium at the surface does not show completely normal layering but it is normally ripened. The same may be seen in the network of epithelial strips. Where these are cut tan-

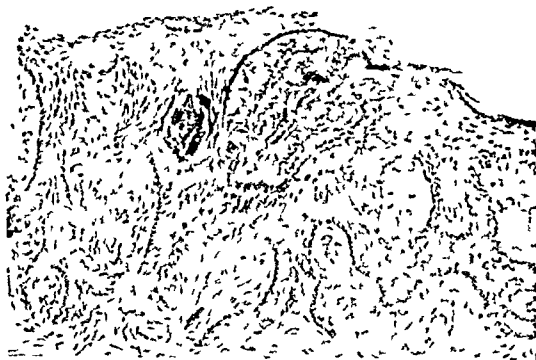


Fig 6 Part of a benign, warty papilloma of the portio

gentially the basal cells look abnormal partly spindle shaped. The latter occurs when pressure of the growing connective tissue forces the epithelium to form cords with sharply demarcated edges and points.

Many cases similar to these demonstrated have been incorrectly diagnosed as malignant. Such errors can and must be avoided and this will be aided by careful laboratory handling of the tissue. An experienced person will seldom have difficulty in interpretation of the findings although at first glance it might appear that the epithelium is independently invading the underlying tissue. Serial sections will show that all of these processes lie in what were originally glands. Diligent search will reveal the persistence of gland lumina and mucous epithelium.

It must be remembered that gland lumina and mucous epithelium can be seen in the presence of invading carcinoma and that the carcinoma may invade the glands. Thus

attention must be given to the character of the epithelium in the glands. In the majority of cases the epithelium of cervical carcinoma may be readily differentiated from that of erosion healing and polyps. Carcinoma cells show deviations from the normal which are particularly evident in the nuclei. The chromatin content is increased and the nuclei are more darkly stained. The size of the nuclei is increased without comparable increase in the cytoplasm. The shape of the nuclei is irregular. The general conformation of the normal epithelium is lost leading to absence of a special basal cell row and loss of regular layering. Anomalies of mitosis seldom occur in the early stages of carcinoma. The basal membrane is often intact in the early stages and is destroyed as the disease advances. These details will be discussed in a subsequent paper which will also include details of the literature to which reference has been made in this article.

# THE MANAGEMENT OF THE JAUNDICED PATIENT

## With Special Reference to Vitamin K

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THE mortality accompanying operations on jaundiced patients has long been augmented and sustained by the incidence of postoperative hemorrhage. A recent analysis of 4,000 operations on jaundiced patients reveals 16 per cent of the fatalities to be due to postoperative hemorrhage (15, 16). This complication has long remained an enigmatic problem and it is only through an increased knowledge of the importance of nutrition, that an effective means is at hand to combat this dreaded sequel to operations for obstructive jaundice. There is perhaps no field of medical research in which more rapid progress has been made than in the science of nutrition. In the early part of the present century it was felt that protein, carbohydrate, fat, minerals, and water were the essential elements to promote growth and development. However, the increasing knowledge of vitamins reveals that they play an important rôle in the state of general nutrition, cardiac reserve, resistance to infection and in certain other functions such as the prevention of hemorrhage and the healing of wounds. Important recent contributions in the study of nutrition concern the rôle of vitamin K in the prevention and treatment of the hemorrhagic diathesis associated with the various forms of obstructive jaundice. Fortunately there was general agreement that the hemorrhagic diathesis of jaundice is due to a lowered prothrombin level of the blood almost simultaneously with the discovery of vitamin K by Dam of Copenhagen. He found that a fat-free diet would produce enormously prolonged clotting-time in dogs. It then developed from further studies that the addition of a certain fat-soluble substance found in hog's liver and in spinach and

other green vegetables would prevent this hemorrhagic tendency. This substance was designated as vitamin K from the Danish word "Koagulation." Subsequent studies by Dam (6 to 11) and others, notably Almquist (1 to 4), have demonstrated that vitamin K is present in the photosynthetic portions of certain plants and that it is produced by bacterial activity in the intestine of man.

Avitaminosis K is manifest clinically in a tendency to bleed due to a lowered *prothrombin level* of the blood. It is generally agreed that the blood of jaundiced patients is not deficient in calcium, fibrinogen, or platelets. Likewise there is no evidence that the presence of bilirubin in the blood has any adverse effects on its coagulating propensities *per se*. A review of the factors concerned in normal blood coagulation will demonstrate the rôle of prothrombin (12).

Recent studies continue to support the thrombin theory which holds that a coagulant, thrombin, is formed from an inactive precursor, prothrombin, through the agency of calcium salts and thromboplastic factors (Fig 1). Thrombin in turn converts fibrinogen into fibrin.

**Fibrinogen.** Plasma fibrinogen is a globulin-type of protein formed by the liver and is always present in the circulating blood. Preparations of this substance are usually obtained by salting-out with neutral salts and they may be lyophilized for preservation in the dry state. Repeated quantitative studies of the fibrinogen in the blood of jaundiced patients show no consistent abnormality. The fibrinogen level has been used as an index of liver dysfunction (18).

**Thrombin.** This substance plus fibrinogen results in the formation of a fibrin clot. Intravascular clotting is prevented by the fact that thrombin is never present in the circulating blood, but is formed from its inactive pre-

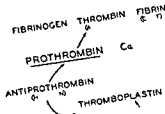


Fig. A diagram to represent the way of blood coagulation which holds that a precursor (prothrombin) is formed from a natural precursor (prothrombin) through the agency of calcium ions and thromboplastin. Thromboplastin converts fibrinogen into fibrin. Thrombin turns prothrombin into thrombin. Thrombin is produced by the activation of prothrombin (heparin). Extra-vascular clotting occurs through neutralization of the prothrombin effect by the thrombolytic factors (platelets and tissue).

cur or prothrombin (thrombogen) It is highly potent and has been employed for local hemostasis (24)

The initiation of blood clotting—union of fibrinogen and thrombin to form fibrin—appears to be dependent upon two substances. Antiprothrombin Antiprothrombin or heparin prevents thrombin formation from prothrombin. It is an inhibitory substance probably formed in the liver normally found in the blood and contains mucotinic polysulfuric, acetic and glycuronic acids. Purified products differ in anticoagulant potency.

**Thromboplastin** Crude aqueous tissue extracts are rich in this substance and possess powerful clot aiding properties. Thromboplastin factors come from plasma itself as well as from platelets, tissues—including brain, lung, placenta and bone marrow—and secretions. Chemically thromboplastin is a phospholipid and is not available until mobilized. The analysis of Ferguson and Erickson (13) reveals a proteolytic thromboplastin enzyme analogous to crystalline trypsin as the mobilizing factor. These substances when liberated presumably fix the antiprothrombin thus releasing its inhibitory effect upon prothrombin.

An extravascular clot is composed of a meshwork of fibrin thread between which are found red and white blood corpuscles. When a wound occurs mobilization of the thromboplastin factors at the site of tissue injury results in the fixation of the antiprothrombin—heparin. In turn the inhibitory

## METABOLISM

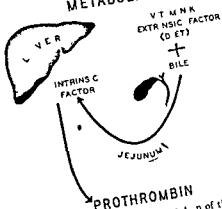


Fig. A diagram to represent the way of blood coagulation which holds that a precursor (prothrombin) is formed from a natural precursor (prothrombin) through the agency of calcium ions and thromboplastin. Thromboplastin converts fibrinogen into fibrin. Thrombin turns prothrombin into thrombin. Thrombin is produced by the activation of prothrombin (heparin). Extra-vascular clotting occurs through neutralization of the prothrombin effect by the thrombolytic factors (platelets and tissue).

effect upon the prothrombin is released thus leaving it free to be activated by calcium ions with transformation into thrombin. The newly formed thrombin promptly unites with the available fibrinogen to form fibrin which entraps the blood corpuscles and later contracts to form a clot (Fig. 1)

It has been emphasized that the blood of jaundiced patients possesses one variable factor in this chain of events. The thromboplastin factors are ample and a fibrinogen deficiency is an extremely rare cause of bleeding. Evidence that the heparin content of the blood may be increased is lacking. The clotting time of blood on recalcifying is a value of added thromboplastin is a value which under standardized conditions affords a relative estimate of the prothrombin content. These values—prothrombin clotting activity—are consistently low as obtained from the blood of jaundiced patients who demonstrate a bleeding tendency.

A brief summary of the current state of our knowledge with respect to the so called bleeding tendency is supplied by Ferguson (1). Bleeding involves positive causative factors as well as failure in control. Coagulation defect are an important aspect of the latter but the former includes special fac

tors such as the susceptibility of capillaries to injury. Fibrinogen deficiency is an uncommon cause of bleeding, usually associated with gross liver injury. Pseudohemophilia is a fibrinogen deficit and may be hereditary. Prothrombin lack has recently leaped into prominence. It is due either to liver damage or to an inadequate supply of vitamin K, generally because of failure of intestinal absorption in biliary disorders. For calcium insufficiency to be a significant cause of hemorrhage, the diffusible serum calcium would have to fall below the lowest recorded level compatible with life. Thromboplastin defects offer the clue to the clotting delay in true hemophilia. Heparin and antiprothrombin increase may explain conditions such as the anaphylactoid purpuras when associated with incoagulability of the blood."

The exact nature of prothrombin has not been elucidated but its preparations contain globulin protein which may be precipitated by dilution and acidification. Like other plasma proteins, prothrombin is formed in the liver and is therefore a manifestation of normal liver function. The Quick test of the prothrombin activity of the blood is an index of liver dysfunction and parallels the hippuric acid test (25).

The chain of events which perhaps transpires in the formation of prothrombin may be depicted diagrammatically (Fig 2). The metabolism of this substance is intimately concerned with the proper utilization of vitamin K. The fat-soluble factor K—which is present in the photosynthetic portion of plants and may be produced by bacterial activity—possessing the solubility properties of fats must have *bile* for its emulsification and absorption. Absorption is thought to occur primarily in the jejunum. The extrinsic factor thus emulsified and absorbed theoretically unites in an obscure way with an intrinsic factor in the liver affecting the synthesis of *prothrombin*. The latter is apparent from the ease with which the prothrombin level of the blood may be reduced to hemorrhagic levels by the administration of hepatotoxic substances, such as carbon tetrachloride. The general effects of bile on the absorption of fat-soluble vitamins have been well demonstrated by

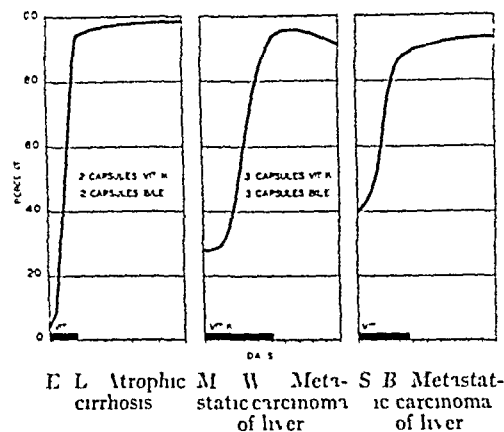


Fig 3 Case L L No 439,527 Obstructive jaundice from advanced cirrhosis of the liver with ascites. A rise in the prothrombin clotting activity from 5 per cent to 95 per cent in 12 hours with two doses of vitamin K. Case M W No 453,204 Advanced metastatic carcinoma of the liver. Obstructive jaundice with prompt rise in prothrombin clotting activity. Case S B No 458,740 Advanced metastatic carcinoma of the liver retaining the ability to synthesize prothrombin.

Greaves and Schmidt, who have shown that deoxycholeic acid is essential for proper absorption of carotene, vitamins D, E, and K. Since sterile bile does not contain the vitamin and since infected bile contains only small amounts of it, it is apparent that bile exercises its beneficial effect only by facilitating the absorption of vitamin K, normally present in the intestinal tract. Likewise the addition of bile and vitamin K to whole blood has no enhancing effect on its coagulability.

From the diagram, it may be seen that in order that a normal amount of prothrombin shall be present in the blood, vitamin K must be absorbed and utilized by the liver. This is dependent on three primary requisites: (1) there must be physiologically active bile participating in the normal digestion of fat, (2) there must be an adequate absorptive intestinal surface, (3) there must be a physiologically active liver. It is probable that the dietary factors may be minimized inasmuch as the bacterial activity occurring in the intestine produces vitamin K. The vitamin can also be prepared from fish-meal after the extracted material has been allowed to putrefy. Almquist and his associates have isolated a fish-meal organism which closely resembles





Fig 4 left C E L (Fig 3) B p y f l  
Lo p m g fcat B t mi tai sh b  
type l atr ph h b Cas S B (Fig 3) Biopsy

of l e L w p w m en hatio h m t yl d  
t sho ng r pl m t d at phy f d  
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*Bacillus cereus* and is capable of synthesizing considerable amounts of vitamin K. The vitamin is also present in *Escherichia coli* *Bacillus subtilis* *Staphylococcus aureus* and many other micro organisms including *Mycobacterium tuberculosis* presumably contained in the lipid fraction of the organism. A avitaminosis in man then is not so much a deficiency disease as it is a condition due to faulty absorption. There are numerous clinical conditions other than jaundice which may alter the metabolism of prothrombin so that spontaneous hemorrhage ensues. Hypoprothrombinemia has been observed in gastrocolic fistulas in which the jejunum is completely side tracked and absorption therefore impaired. For the same reason abnormal bleeding tendencies have been demonstrated in patients with intestinal obstruction acute gastric dilatation sprue ulcerative colitis and following certain side tracking operations such as an ileosigmoidostomy. The most frequent condition however which predisposes to a lowered prothrombin level is the absence of bile in the intestine accompanying obstruction of the common duct by neoplasm stricture stone and in complete biliary fistulas. Theoretically cirrhosis of the liver hepatitis or replacement of the hepatic parenchyma with neoplasm will so interfere with physiological activity that the metabolism of prothrombin will be impaired. Practically how

ever it would seem that such a condition is rare due to the fact that nearly 85 per cent of the hepatic parenchyma must be destroyed before signs of severe insufficiency are apparent.

For the past 18 months vitamin K or one of its related compounds has been administered on the general surgical services for the prevention of postoperative bleeding in jaundiced patients. Inasmuch as the indication for the administration of this substance is a lowered prothrombin level of the blood vitamin K cannot be given intelligently without following the patient's blood carefully with one of the prothrombin tests. At the University Hospital both the Quick and the test for presumptive determination of the amount of prothrombin present as developed by Smith et al have been employed. The latter is now being employed exclusively because of its increased ease of performance. It is an excellent clinical test of a patient's tendency to bleed and the results check well with those obtained by other more complicated methods. It has been completely satisfactory in our hands on over three hundred occasions. These presumptive tests are based on the fact that the addition of thromboplastin to blood initiates the primary phase of coagulation with conversion of the physiologically inactive prothrombin to the active thrombin. Where the prothrombin is appreciably lowered the

blood will not clot normally even in the presence of an excess of thromboplastin. The thromboplastin is easily obtained by grinding one rabbit lung in a mortar and pestle with sterile sand along with 15 or 20 cubic centimeters of physiological saline. After thorough grinding the solution is allowed to stand overnight in an icebox and in the morning may be strained off through gauze. This fluid is a rather crude aqueous extract of the thromboplastic factors and is ready for use. The aqueous extracts obtained in this manner are more potent than the equivalent of their isolated phospholipids. One tenth of a cubic centimeter of this substance when added to one cubic centimeter of normal blood will cause rapid clotting in from 15 to 30 seconds. The latter value is more desirable as it is easier to work with. The blood of a patient with hypoprothrombinemia on the other hand is greatly prolonged in its clotting activity in spite of the addition of this excess of thromboplastin. The clotting activity as measured by this method is expressed in percentage of normal by dividing the normal value by the abnormal and multiplying by one hundred. If the value obtained in this manner is below 40 per cent, the patient is considered to be in danger of bleeding. Thromboplastin solution prepared in this manner has remained active for as long as 7 weeks. It is kept in an icebox in a general utility room and is available to the internes at all times. The test is always done on a "normal" to provide an accurate biological assay of the potency of the solution. It slowly loses its activity in a variable length of time due to the variable rate of decomposition.

Thromboplastin is obtainable in a desiccated form in ordinary capsules<sup>1</sup> which produces a solution possessing an apparent high degree of uniformity. We have found that this solution clots normal blood in from 25 to 30 seconds. When used on blood with a low prothrombin level it gives values which check well with those obtained from the thromboplastin solution made directly from rabbit lung. This new preparation obviates the necessity of the extraction process and should prove convenient when there is only an occasional necessity for performing these tests.

It should be emphasized that the conventional bleeding tests of Duke and Ivy are not to be relied upon in detecting *hypoprothrombinemia*, as normal values may be obtained by these methods when a test of the prothrombin activity will show the patient to be in imminent danger of bleeding.

This test has been done in many other conditions in which there is a bleeding tendency such as congenital hemolytic icterus, idiopathic thrombocytopenic purpura, hemophilia, and other blood dyscrasias. Normal values for the prothrombin clotting activity are obtained inasmuch as there is a normal amount of prothrombin in these conditions. This stresses the important fact that the only true indication for the administration of vitamin K is a lowered prothrombin level of the blood. The administration of vitamin K for menorrhagia, metrorrhagia, and essential hematuria is a waste of time for the same reason. However, encouraging results have been obtained in the hemorrhagic disease of the newborn, since a definite hypoprothrombinemia has been demonstrated from the second half of the first to the sixth day of newborn life (23). Infants with hemorrhagic disease may have a prothrombin level as low as 5 per cent of normal and the administration of vitamin K is as dramatic in its results as whole blood.

A case recently encountered in the University Hospital suggests another important factor which may predispose to hypoprothrombinemia.

F. R., aged 63 years, white male was admitted on February 19, 1940 with a three year history of nocturia, polyuria, and diminution in size and force of urinary stream. Physical examination revealed a well developed rather obese elderly male who did not appear ill. The general examination was entirely normal except for a 2+ benign enlargement of the prostate gland. Laboratory studies showed a negative blood Kahn, heavily infected urine, hemoglobin, 85 per cent, white blood cells, 12,500, and a nonprotein nitrogen of 43.8 milligrams per cent. Transurethral prostatic resection of 30 grams of benign tissue was done on February 21, 1940. The postoperative course was characterized by a series of complications. On the third postoperative day he became very distended with x-ray evidence of intestinal obstruction which was relieved by intestinal intubation. A cardiac irregularity then developed which improved following digitalization. The pa-

<sup>1</sup>ParLe Davis and Co

tient gradually rallied from this episode but on March 10 1940 he began to have massive gastric hemorrhages and promptly went into shock. The hemorrhage continued and during the 4 remaining days of his life he was given a total of 3 200 cubic centimeters of citrated blood in addition to 7 500 cubic centimeters of intravenous fluids—an estimated volume for volume replacement. The hemorrhage continued and on March 12 1940 a test of the prothrombin clotting activity was done. A mushy clot formed in 20 minutes while the thromboplastin solution was found to clot normal blood in 20 seconds (1.6 per cent of normal). In the following 24 hours 12 000 curative units of vitamin K<sub>1</sub> and 4 grams of bile were given by stomach tube drip and on the following day the patient's blood would clot in 30 seconds—60 per cent of normal. The bleeding from the stomach promptly decreased but signs of pulmonary consolidation had appeared. The death on March 14.

This case is of theoretical interest because none of the usual criteria which predispose to hypoprothrombinemia were present. He had been taking a normal diet there were no known abnormalities in the biliary tract and there was no evidence of hepatic insufficiency. The tremendously prolonged clotting activity which was restored to approximate normal values—from 1.6 per cent to 60 per cent—in 4 hours would likewise preclude the possibility of any generalized impairment of liver function. A postmortem examination showed that exsanguination had occurred as a result of massive hemorrhage from an artery at the base of a subacute gastric ulcer. Multiple recent esophageal and gastric ulcers were also noted. Patchy retrogressive chemical changes were noted in the liver. The biliary duct system was patent. Therefore it seems that depletion of the prothrombin reserve occurred as a result of repeated dilution of the blood with saline and glucose in the presence of sustained hemorrhage. Even though 3 200 cubic centimeters of fresh citrated blood was given it is significant that after transfusion as with *in vitro* experiments prothrombin increase is simply additive. After exhaustion of the liver reserve of prothrombin had occurred synthesis from available vitamin K in the intestinal tract was prevented by aspiration of the bile as a result of the constant gastroduodenal suction. In such an instance when there is repeated hemorrhage such as in bleeding ulcer with replacement by parenteral fluids

the relative amount of prothrombin may become so diluted that an abnormal incoagulability develops. Prolonged gastroduodenal drainage by suction is likewise not without danger due to the continuous aspiration of bile. During the past year 3 cases have been observed in which a severe hypoprothrombinemia developed in instances in which the only predisposing factor was the continuous aspiration of bile from the gastrointestinal tract with the suction apparatus. One illustrative case report follows.

M. T. aged 36 years No. 451769 was admitted to the hospital February 26 1940 for treatment of an obstructing neoplasm in the sigmoid colon. Complete obstruction was treated by repeated intravenous fluids gastroduodenal suction and cecostomy on February 27. His convalescence was satisfactory until March 7 when he suddenly began to bleed from the cecostomy wound and rapidly went into shock. He failed to respond to blood transfusions morphine oxygen and heat. A test of the prothrombin clotting activity shortly before death gave a value of 30 per cent of normal. Six thousand units—6 capsules—of vitamin K with 2 grams of bile were given by stomach tube and in 4 hours the prothrombin activity was 72 per cent of normal and the bleeding had dramatically decreased.

These 2 cases stress the fact that there are a wide variety of clinical conditions other than jaundice which may so interfere with the metabolism of prothrombin that an abnormal bleeding tendency develops. Repeated administration of intravenous fluids in the presence of hemorrhage and the continued aspiration of bile from the gastrointestinal tract are certainly indications for performing tests of the prothrombin clotting activity of the blood.

The conception that no response can be obtained from the administration of vitamin K in cases with extensive intrinsic liver disease seems rather firmly established. Cases with cirrhosis and low prothrombin level presumably are poor candidates for the administration of vitamin K. This analogy is further supported by the fact that prothrombin levels fall in experimental animals with hepatitis of chloroform origin. Experiences with this type of patient at the University Hospital have led to the conclusion that such a condition is rather rare. Figure 3 illustrates three examples in which a completely satisfactory

response in the blood was obtained by the administration of vitamin K and bile in the presence of extensive intrinsic liver disease. In all 3 instances there was marked reduction in the prothrombin clotting activity.

E L, No 439527, aged 38 years, was admitted to the hospital with painless obstructive jaundice on October 31, 1939. The prothrombin activity was only 5 per cent of normal but after two doses of vitamin K and bile, it rose to 95 per cent in 12 hours. Laparotomy revealed a large amount of ascitic fluid and the biliary duct system was patent. The liver was dark, markedly enlarged and grossly cirrhotic. A biopsy specimen was taken and reported as atrophic cirrhosis. Figure 4 shows a photomicrograph of the biopsy specimen.

M W, No 453294, aged 48 years, was admitted on the surgical service with deep obstructive jaundice. A large mass was palpable below the costal margin on the right suggesting the possibility of carcinoma of the head of the pancreas, common duct, and gall bladder, the latter being favored because of a history of long standing cholelithiasis. The prothrombin activity was 28 per cent of normal and after preparation with vitamin K and bile it rose to 95 per cent. At the time of laparotomy, there was considerable ascitic fluid, and the gall bladder was enlarged, hard, and extremely fixed to the adjacent structures. There were extensive metastases in both lobes of the liver, approximately 50 per cent of the liver being grossly replaced by neoplasm. A palliative operation was not undertaken.

S B, No 458740, aged 48 years, was admitted to the hospital with persistent jaundice of varying intensity for 4 years. A cholecystectomy had been done in 1937 for cholelithiasis and a second operation in 1939, without successful exploration of the common duct. The liver was at least 10 centimeters below the costal margin, firm, and somewhat nodular. The prothrombin activity improved from 40 to 87 per cent of normal in 3 days, with the administration of vitamin K and bile. At laparotomy the liver was found to extend to the brim of the pelvis almost filling the entire abdomen. It was virtually filled with large umbilicated nodules of metastatic carcinoma. Hemostasis was well controlled throughout the procedure, a biopsy specimen was taken and the wound was closed. Figure 4 illustrates the pathological findings in the liver.

In these 3 cases, 2 of metastatic carcinoma of the liver and 1 of extensive cirrhosis with ascites, rapid and satisfactory responses were obtained in the clotting activity of the blood following the administration of vitamin K. Hemostasis was easily accomplished at operation in each case. This is somewhat contrary to the conception that intrinsic liver disease, such as cirrhosis, will markedly impair the

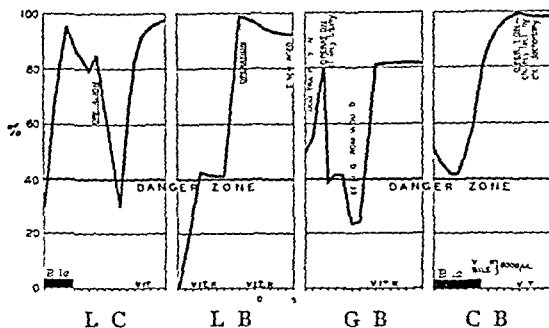


Fig 5 L C No 453,340 November 26, 1940, obstructive jaundice, hepatosplenomegaly, cholelithiasis, choledocholithiasis. Prompt rise in prothrombin clotting activity from sole administration of bile only to fall rapidly following operation. Second sustained response from Vitamin K and bile. L B No 450,758 September 27, 1939. Cholecystectomy, April, 1938. Plastic to common duct, October, 1938. Recurrence of jaundice, February, 1939. Severe hemorrhagic diathesis, hematomas of abdominal wall following simple palpation, prolonged bleeding from excoriation of pruritic areas. After vitamin K therapy, operation with normal hemostasis—usual postoperative fall in prothrombin prevented with prompt resumption of vitamin K therapy. G B No 448,195 August 11, 1939. Carcinoma of pancreas with carcinomatosis, jaundice, 4 weeks' duration. Transient effects of blood transfusion of the prothrombin level. Rapid postoperative fall with bleeding from the wound after operation, promptly controlled with vitamin K. C B No 220,097 December 13, 1939. Obstructive jaundice, cholelithiasis, choledocholithiasis. Conditioned with bile alone with a satisfactory response. Further reinforcement of the blood was accomplished with 6 doses of vitamin K the day before operation, thus preventing the postoperative fall observed in cases L C and G B.

metabolism of prothrombin. It is interesting that in this case only 2 capsules of vitamin K were given followed by a rise from 5 to 95 per cent of normal in 12 hours. Inasmuch as Ivy has shown in the experimental laboratory that close to three-fourths of the hepatic parenchyma must be destroyed before signs of severe insufficiency are manifest, it is not surprising that propensities for synthesizing prothrombin may be retained in such instances.

The crude extracts of vitamin K<sub>1</sub> have been employed in these studies along with the newer highly soluble forms of bile which have been desiccated in vacuum. The dosage that seems to be universally satisfactory is one capsule—1000 curative units, Thayer-Doisy method—with 1 capsule—0.32 gram—of bile 3 times a day. When the oral route cannot be utilized, this mixture is given by drip in sus-

<sup>1</sup> Vitamin K in oil—P. Le-Davis and Co.

pension with a stomach tube. In many instances the normal metabolism of prothrombin may be restored by giving bile alone. Case L C and C B in Figure 5 illustrate the remarkable improvement that may be obtained in the prothrombin clotting activity by the administration of bile alone. This makes it apparent that it is extremely difficult to evaluate individually the efficacy of certain of the synthetic preparations when they are given with bile. Attempts to evaluate comparatively certain of the new synthetic preparations such as methyl 1,4 naphthoquinone have not been conclusive. The beneficial results frequently observed in the past from viosterol (5) undoubtedly may be attributed to the bile which was always given with it. We have encountered one patient who did not improve on quinone therapy but showed remarkable improvement when vitamin K<sub>1</sub> in the crude form was given. Rhoads and Fliegelman (20) used 2 methyl 1,4 naphthoquinone in the treatment of prothrombin deficiency in 10 patients. One case in this series likewise failed to respond to the oral administration of the synthetic vitamin but improved rapidly when the crude product was given orally.

It is evident at once in studying these patients that the immediate postoperative period requires careful watching as there is often a marked drop in the prothrombin level which is thought to be due to utilization of prothrombin in the wound, loss of blood, anesthetic agent and trauma to the liver. The postoperative fall which has been so dangerous in the past may be prevented by an adequate preoperative preparation. Cases L C and G B illustrated in Figure 5 are two examples in which there was a rapid fall in the prothrombin activity following operation and in each instance serious complications were averted by the administration of vitamin K<sub>1</sub>. In one of the cases there was bleeding from the wound which promptly stopped. It should be noted that this case was not prepared with vitamin K<sub>1</sub> but rather with two blood transfusions. After transfusion prothrombin increase is simply additive and the beneficial effects may last as little as 1 hour. This is borne out here in that there was a rapid fall

in the prothrombin resulting in hemorrhage from the wound on the third postoperative day. Conserved blood loses approximately 50 per cent of its prothrombin in 5 or 6 days and therefore should not be used for this purpose when other sources are available (21). The usual postoperative fall has been prevented in Cases L B and C B by the administration of vitamin K<sub>1</sub> up to the time of operation. Eight patients have been encountered who may be classified as desperate risks from the standpoint of their marked bleeding tendency. One of these patients L B was observed to soak an entire towel with blood in an attempt to stop the intractable hemorrhage from simple excoriations of pruritic areas. In every instance they have had a convalescence completely free from bleeding after preparation with vitamin K<sub>1</sub>. There have been several with normal or slightly increased Ivy bleeding times who were later shown to be in the danger zone with a test of the prothrombin activity.

#### SUMMARY

The mortality accompanying operations on jaundiced patients may be materially reduced by careful attention to the details of preoperative and postoperative care. The incoagulability of the blood frequently observed in this group of patients is due to a prothrombin deficit. Prothrombin is one of the serum proteins and like other serum proteins is supplied by the liver. A prothrombin test therefore is simply a test of liver function and parallels other tests as an index of liver dysfunction. Avitaminosis K<sub>1</sub> is not so much a deficiency disease as it is a condition due to faulty absorption and is responsible for a demonstrable fall in the blood prothrombin which is manifest clinically in a tendency to bleed. The most common cause of hypoprothrombinemia is the absence of bile in the intestine, a condition common in the various forms of obstructive jaundice and other related conditions. Repeated administration of intravenous fluid in the presence of hemorrhage and the continued aspiration of bile from the gastrointestinal tract by the Wangenstein suction apparatus are conditions where a test of the prothrombin clotting

activity should be done. The usual bleeding tests of Duke and Ivy are not dependable in detecting this deficiency, while the bedside test of Smith has proved to be highly satisfactory for clinical purposes. The fact that the prothrombin level of the blood may be reduced to hemorrhagic levels by the administration of hepatotoxic substances makes it apparent that the liver plays an important rôle in the metabolism of prothrombin. Clinically, it would appear that the ability to synthesize prothrombin may be retained in a certain number of cases even in the presence of extensive cirrhosis and of metastatic carcinoma of the liver.

Therefore, as in the past, the prime objective in the treatment of obstructive jaundice is the restoration of the patency of the biliary ducts and the protection of the hepatic parenchyma. To attain this latter objective, a high protein and high carbohydrate diet should be given. Attention to other vitamin needs will enhance the state of general nutrition, cardiac reserve—vitamin B—resistance to infection—vitamins A and D—and the healing of the wound—vitamin C. Difficult surgical procedures can be successfully accomplished only if bleeding is well controlled. A new light thus shed on an enigma of the past gives hope of materially reducing the risk of surgical operations which are performed upon jaundiced patients.

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# THE CLASSIFICATION OF GASTRIC CARCINOMA

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THE purpose of this paper is to discuss the possibilities of a useful classification of gastric carcinoma. At the present time there is no classification of gastric carcinoma which has been generally accepted or which has a definite bearing on the ultimate prognosis and on the treatment. Study of other tumors formerly considered to be an entity, as for instance brain tumors (1) lung tumors (13) has proved that classification may be useful. Gastric carcinoma practically is considered a uniform entity and few attempts have been made to determine operability, irradiation sensitivity or final prognosis according to types. Microscopic grading has been attempted occasionally, especially according to Broder's criteria, and it has been stated that carcinomas as they are microscopically of grade 1 or grade 2 give a much better ultimate prognosis than the other ones (11).

However from theoretical considerations as well as from the practical experiences it should be obvious that gastric carcinoma is not an entity. It cannot be expected that tumors originating from the surface epithelium will develop in the same way as do those originating from the glands. It is well known that some tumors may grow to a large mass, the size of a fist or even larger, and still give an excellent surgical prognosis, while other tumors prove to be extremely malignant even though they are only a few square centimeters in size. It is not known what makes the difference between these two classes of tumors. From mere speculation one would expect that the microscopic structure would be decisive for the development and ultimate prognosis of a tumor. Such a speculation, however, has to be verified by facts, and this has not yet been done. But it is obvious that microscopic cri-

teria as employed in former descriptions of gastric carcinoma have no relationship either to the macroscopic type or to the ultimate prognosis of the tumor. Sharply walled off tumors which may be operated upon with excellent results may be well differentiated adenocarcinomas and undifferentiated medullary carcinomas as well.

## MICROSCOPIC CRITERIA

The idea that there might be a correlation between the histological structure of tumors and their clinical behavior was considered by Hansemann. With increasing deviation from the normal structure he thought that the malignancy should increase. Broders (3) introduced histological criteria by which tumors might be graded. At first they were applied only to tumors originating from stratified squamous epithelium, but later they were applied to tumors of transitional epithelium (4). Martzloff applied a modified set of criteria to cancers of the cervix uteri, as did Hueper. The grading of epidermoid carcinomas has become firmly established (19, 20).

In the meantime attempts at the grading of cancers of glandular epithelium lagged, although Greenough had made a study of mammary cancer. Stewart and Spie had studied rectal cancer, and Whipple and Raiford had worked on the grading of gastric carcinoma. With the exception of rectal cancer (5) the correlation between deviation from the normal histological structure and the clinical malignancy of glandular tumors was not very great.

Too much credit cannot be given to Haagensen for his critical and scientific approach to the problem of *how criteria for grading* may be established. Instead of grading cancers of the breast according to preconceived ideas as to what histological changes should be given weight, he systematically tested each possible criterion against the known end result in the

patients. By so doing he was finally able to state exactly which changes are evidence of high malignancy. One important result of this approach was that certain changes such as fibrosis, which had been considered to be evidence of resistance to tumor growth, were disqualified as not being important in estimating malignancy, at least in breast cancer. The amazing thing is that this included criteria which had been accepted without serious question but also without scientific testing, as valid since the beginning of the microscopical study of tumors, about a hundred years ago. In retrospect the error is clear. It is a psychological carry-over, without question, of what is known to be true in infectious disease and repair, in which process fibrosis is usually evidence of resistance on the part of the host. Haagensen similarly disqualified other criteria which had previously not been tested critically.

A preliminary grading of about two hundred gastric cancers has been made by us, without having recourse to the critical testing of the validity of criteria, which Haagensen used. Our experience showed that by the use of preconceived standards of malignancy, to be cited, gastric cancer could not be profitably graded histologically. There was no important difference in the histological grade of tumor in 8 patients whose clinical course from the onset of symptoms to death covered less than 2 months, when compared with a group of 12 patients whose clinical course covered 18 months or longer. That there was no correlation between the grouping of these patients when compared with their macroscopic type will be discussed later.

In the histological grading of these gastric carcinomas the main reliance was placed on the degree of deviation from the normal gastric gland structure. Additional evidence, which was used in the finer grading, was derived from a study of the degree and manner of infiltration of the carcinoma into the true muscle layers and also from the nature of its lateral growth as seen at the advancing margins. This latter point is closely related to the macroscopic appearance.

The following criteria were accepted for the 4 different grades

*Grade 1* The structure deviates enough from that of normal gastric mucosa and from that of benign polyps to be highly suspicious of malignancy, but proof of malignancy in the form of invasion through the muscularis mucosae or of metastasis is not at hand in the sections examined. Otherwise this is the same as Grade 2.

In other words there is neoplasia minimal anaplasia, but no proof of heterotopia.

*Grade 2* Well formed glands are present although they are increased in size and complexity with some tendency for the cells to pile up, some hyperchromatism of nuclei with an increase in the number of mitotic figures, some loss of basal polarity of nuclei, and some variation in size of nuclei and of total cell size from cell to cell. There is infiltration through the muscularis mucosae or beyond. Secretory activity is variable.

These, then are well differentiated adenocarcinomas showing neoplasia slight anaplasia, and slight to moderate heterotopia.

*Grade 3* The glands are less well perfectly formed and the cells show marked deviation from the normal in arrangement, size, chromatin content, degree of similarity, number of mitotic figures, etc. Focal areas may be almost totally undifferentiated.

These are less well differentiated adenocarcinomas showing neoplasia, moderate to marked anaplasia, and heterotopic growth.

*Grade 4* Glands are extremely poorly formed or not formed at all. The cells are highly anaplastic and organoid arrangements and appearances are nearly or completely lost.

These are highly anaplastic neoplasms showing heterotopia.

In otherwise borderline cases if the advancing margin was sharp the lower grade was given. Similar weight was given if the deep penetration was slight and sharp. Conversely, diffuse widespread infiltration laterally or deeply determined a higher grade, other features being equal.

As mentioned this histological grading apparently failed to correlate with the clinical malignancy, but this apparent failure is not to be interpreted as a condemnation of histological grading. Rather it indicates that our preconceived standards were not adequate to



reveal the malignancy of the cases. Obviously other criteria for the malignancy must be sought and this is now under study. Three or four different types of epithelial cells exist in the stomach. Theoretically each of the *e* has its own cancers although to date they have not yet all been identified. A tumor originating from the mucous neck cells of the gastric mucosa might inherently reproduce tubular glandular structures whereas a tumor composed of gastric parietal cells might grow more solid. Obviously criteria such as the perfectness of gland formation cannot be applied equally to both tumors in grading them. Nevertheless this is what we have been attempting to do in the case of many tumors. The studies of neuropathologists on intracranial tumors indicate that perhaps histological grading of tumors might be more successful if it were preceded by studies on the histogenesis.

Certainly today the fact is well established that it is unwise to attempt to use the criteria which have proved successful in the histological grading of one tumor *in toto* and without critical testing in the grading of a different form of cancer. Furthermore the best criteria can only be established by studying a large number of tumors of each type in relation to the known biological behavior for those tumors.

#### MACROSCOPIC CRITERIA

To the clinician it has been a striking fact that the ultimate prognosis of patients suffering from gastric carcinoma evidently does not depend upon the size of the tumor—in extremely large tumors involving almost the entire stomach treatment sometimes has resulted in complete surgical cure upon the site of the tumor—patients with carcinomas of the cardiac region were cured as were those with carcinomas of the pylorus by early surgery and apparently not upon the microscopic structure of the tumor—highly differentiated tumors although small sometimes lead to early recurrence after surgical interference while apparently very malignant undifferentiated tumors were cured completely. Furthermore striking was the fact that gastric carcinomas grossly have a very varied

appearance which is unrelated to their microscopic structure. It became obvious through prolonged observation that the macroscopic structure is an inherent quality of the tumor itself and does not change during the growth of the tumor. The morbid pathologist was able to find and describe a certain type at autopsy but he did not know whether or not this structure had undergone changes during the lifetime of the patient. The gastroscopist however was able to observe inoperable tumors in patients who refused operation at intervals and came to the conclusion (16) that the gross type of a gastric carcinoma would not change during its life history.

The classical description of the gross types of gastric carcinoma is that of Borrmann which has been widely adopted especially in the description of gastroscopic pictures and which has been used for this study. The rare forms such as canceroids, adenocanceroid, basal cell cancers, carcinosarcomas, chorionepitheliomas and the like have been omitted from the following discussion.

*Type I Polypoid carcinoma.* This type of tumor is characterized by a broad base supporting a hemispherical elevation which is solid and the surface of which consists of numerous nodes of different size. The edge of the growth is sharply limited and often it is overhanging in a mushroom like manner. In the gastroscopic picture it is dark red in color and is often in striking contrast to the surrounding atrophic gastric mucosa which instead of being the orange red of the normal mucosa is gray or greenish gray and may contain visible bluish and reddish blood vessels. At a late stage shallow erosions of the surface of this tumor may develop. It is difficult to differentiate this type of tumor grossly from large benign adenoma. It grows slowly from a bean sized benign looking protrusion to the size of a fist and larger and this development may take 3 years or more. Surgical cures of long duration have been observed in these cases even if the tumor involved almost half of the stomach. Microscopically pictures obtained in this type vary although usually a well differentiated adenocarcinoma is found if the grading described is applied. Often grade 2 and sometimes grade 1 will be found

but it is surprising that in some cases grades 3 and 4 might be observed and that in spite of this fact excellent results from surgery may still be obtained. One of the cases was seen to have developed on the soil of pernicious anemia which had preceded the formation of the tumor by 8 years (See Case 13). In another case histamine proved innocuity and continuous epigastric distress to be interpreted as the symptoms of a chronic atrophic gastritis had preceded the very first appearance of the tumor by 8 years.

The type I gastric carcinoma is found in 2.0 per cent of all cases.

*Type II Noninfiltrating carcinomatous ulcer.* This form consists of an ulcer which is usually rather large. Its floor may be smooth or it may be covered with necrotic tags. Its color as seen in the gastroscopic picture may be a dirty gray or a brilliant white, brownish purplish, reddish hues being frequently present. Sometimes necrotic adherent pieces are seen floating up and down in the current of air introduced during the gastroscopic examination. This ulcer is surrounded by a thick, high usually nodular wall which is limited sharply toward the surrounding gastric mucosa and which slopes steeply toward it. In some cases the wall may be missed at some portions of the edge of the ulcer. But then the growth is still perfectly sharply limited. If the growing of this tumor is observed with a gastrocope it will be seen that the wall may rapidly become thicker, but it has not yet been observed that it ever becomes infiltrative. Until now it seems that it always retains the perfectly sharp limitation even if the tumor grows so large as to involve almost all of the stomach. In most cases metastases are found only at a very late stage and although the tumor may invade neighboring organs as the liver or the colon, even then its advancing border shows sharp limitation. It sometimes is surprising to see what gratifying cures surgery may give in these tumors even if the tumor cannot be called a small one. The microscopic structure varies a great deal. Sometimes grade 2 may be seen but more frequently entirely undifferentiated forms of grade 4 will be found, nevertheless the tumor is not invasive. The surrounding mucosa often differs

from that found in type I. It sometimes seems to be rather normal grossly as well as microscopically. But although this type of tumor frequently has been described as carcinoma originating on the soil of benign ulcer the existence of carcinomatous degeneration in benign ulcer remains to be proved conclusively (14). At the present time it seems that there is no relation between this form and the chronic benign gastric ulcer.

The type II carcinoma has been found in 17.6 per cent of all cases.

*Type III Infiltrating carcinomatous ulcer.* In this type an ulcer is found to lie in the center of a marked elevation. At one side of it a wall may be found which may be either smooth or, more frequently, nodular. It does not slope so steeply toward the normal mucosa as in type II because there is a gradual infiltration into the surrounding mucosa. This wall never surrounds the entire ulcer. At that part of the edge in which no wall is found the ulcer at gastroscopic examination blends gradually with the surrounding gastric mucosa, which then often presents irregular nodes and nodules and stiff infiltration which microscopically are shown to be the result of carcinomatous infiltration. The noninvaded gastric mucosa usually shows definite signs of inflammation. Microscopically all grades and forms may be found. Type III carcinomas occur in 16.3 per cent of all cases.

*Type IV Diffuse infiltrating type.* The gastric wall is diffusely infiltrated and neither with the eye at gastroscopy nor at the inspection of the gross specimen, nor by palpation will any sharp limitation be found anywhere. Shallow or deep ulcerations are frequent, and gastroscopic as well as x-ray examination teaches that such ulcers may heal for some time, other ulcers developing at other places of the carcinomatous infiltration. It seems that this type of tumor starts as a diffusely infiltrating one and that it has no tendency at any time to become limited. Microscopically while all forms and types may be found, undifferentiated forms are the most frequent. Occasionally even a grade 1 carcinoma may be seen which belongs to the gross type IV.

This type occurs in 63.2 per cent of all cases.



Fig. 1. Gross specimen of a polypoid carcinoma of the stomach, showing a large, irregular, and lobulated mass protruding from the gastric mucosa.



Fig. 2. Microscopic section of the tumor tissue, showing glandular structures and cellular details characteristic of adenocarcinoma.

In addition to this description two points should be mentioned namely that Konjetzny subdivided the type IV into the 2 groups taking out from the Borrmann classification those cases in which the entire stomach is infiltrated (leather bottle stomach). Further more the authors are not convinced yet that in the future the types III and IV will have to be separated. It is possible that their clinical behavior is alike and in contrast to the type I and II carcinomas. Perhaps only a type III should be used in descriptions of gastric carcinoma namely that group which infiltrates diffusely.

### CASE REPORTS

In order to give an idea of the different prognoses and development of these forms 3 case histories will be rendered briefly of a type I, II and IV carcinoma respectively.

**CASE I.** This case has been briefly described elsewhere (15) (No. 32830). A 58 year old male developed pernicious anemia in April 1926 and responded well to liver therapy. In November 1926 a gastric tumor was demonstrated at x-ray examination. A pedunculated polyp 6 by 4 by 5.3 centimeters was

removed and the base was cauterized. Sections of the polypoid adenocarcinoma but no tumor cells were found in the pedicle. The patient continued well under liver therapy. In the spring of 1934 the patient noted unusual hunger which occurred before meals and before bedtime and which was relieved by the taking of food. X-ray examination disclosed a polypoid intraluminal mass. A subtotal gastrectomy was performed in June 1934 by Dr. Dallas B. Hester. A large fungating mass was found on the greater curvature of the stomach. The gross specimen shown in Figure 1. The bulk of the tumor consisted of microscopic cavities (Fig. 2) of many regular tubules with several layers of cells. The nuclei of these cells are rather pale and irregular. Many mitoses are seen. In many places of this section there are no tubules but coherent sheets of carcinomatous tissue. The mucosa adjacent to the tumor contains tremendous lymphocytic infiltration and proliferation of the surface epithelium and some atrophy. At a distance from the tumor the epithelium is atrophic. The Brunner glands are well developed but extensive pathological lymphocytic infiltration with enlarged lymph follicles is seen very rarely. At

With this history this exceptional case. D. W. L. Palmer



Fig 3 Microscopic section taken from the surroundings of the polypoid type I, grade 3, tumor pictured in Figures 1 and 2. In this section there is definite atrophic gastritis present, the gastric glands are reduced in amount and the gastric mucosa is thinned with extensive small cell infiltration, especially at the left border of the picture. At the right border of the picture Brunner glands penetrate the muscularis mucosae without presenting any signs of malignancy.

several places the Brunner glands penetrate through the thickened muscularis mucosae and reach into the submucosa without showing any malignant changes (Fig 3). Some apparently normal Brunner glands are seen isolated within the submucosa. But at one place at which the Brunner glands penetrate the muscularis mucosae, also, there is a definite malignant degeneration exactly at the level of the muscularis mucosae, and from there many carcinomatous tubules spread within the submucosa (Fig 4). Here the carcinoma has a different aspect, the lumen of the tubules is wider than in the other sections. The cells lining the lumen are flat, containing more chromatin than those described before, and the wide lumina contain colloid substance. In these pictures one gets the impression of a multicentric origin of this carcinoma. On the other hand, within the mucosa the limit between the tumor and the noninvaded mucosa is perfectly sharp (Fig 5). The lymph glands are not invaded, but carcinomatous tubules are seen in the mesentery.

This obviously is a type I carcinoma which microscopically presents various pictures, if grading were attempted this should be called a grade 3 carcinoma. Nevertheless, the patient is still alive 7 years after the removal of the tumor.

CASE 2<sup>1</sup> In 1935 Dr S. S. Berger saw this patient because of repeated hemorrhages and found at examination a carcinoma which involved practically the entire stomach. In spite of this fact he decided to give the patient a chance and referred him for surgery. A total gastrectomy was carried out by Dr

<sup>1</sup>We owe this remarkable case to Dr Samuel S. Berger of Cleveland. We are indebted for the pathological material and description to Drs A. A. Berg and Paul Klemperer, both of New York.

A. A. Berg, of New York. The stomach was removed from the cardiac end at the junction with the esophagus on the right across the top of the fundus leaving a small siver of the fundus of the stomach for anastomotic purposes. This procedure was performed on January 31, 1935. The patient was alive and in good health on September 11, 1940, 5½ years later.

Dr Paul Klemperer reported that according to the macroscopic description the tumor was sharply limited grossly. On microscopic sections the gastric mucosa does not look definitely atrophic. There is some infiltration between the body glands consisting especially of plasma cells. The sharp limitation of the carcinoma is very well seen in the microscopic section (Fig 6). The tumor is surrounded by a large area of inflammatory tissue containing numerous leucocytes and lymphocytes with the production of a kind of wall of connective tissue. The carcinoma itself is an alveolar adenocarcinoma, highly differentiated, however. The cells of the tubules are of a very irregular size lying often in several layers. The nuclei are of rather irregular shape and size with little chromatin. The lymph glands are not involved.

This carcinoma could be called a grade 2 carcinoma microscopically. We consider the case as characteristic of a type II Borrmann carcinoma. Although it involved the whole stomach it was grossly and microscopically sharply limited, and total gastrectomy led to a five year cure.

CASE 3 This case has been reported elsewhere with pictures of the roentgenological findings, gross specimen, and microscopic findings (17). But the outcome of the case was not yet known at that time.



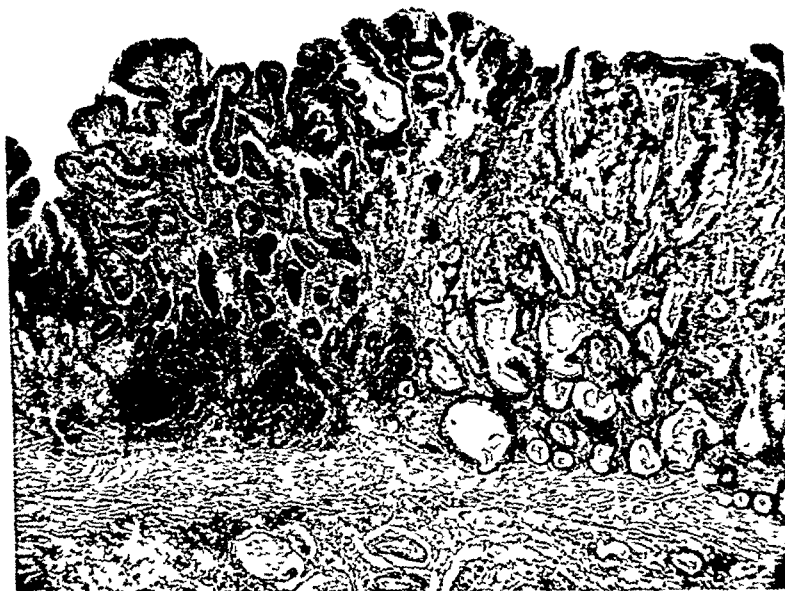


Fig 5 Microscopic section through the edge of the type I, grade 3 carcinoma pictured in Figures 1 and 2. At the left side inflamed gastric mucosa is seen. At the right side the tubular carcinoma is demonstrated. The limit is a perfectly sharp one.

macroscopic types. However, 21 of 23 type IV carcinomas belong microscopically to grade 4. It naturally was not possible to have a complete follow-up of all these cases. Some of them died after the operation, and in others the time elapsed since the operation is not long enough to permit any conclusions. It seems to us rather characteristic, however, that 2 patients who had suffered from type I carcinomas are still alive, the one after a period of 7 years and the other after 2½ years, that 1 of the grade 2 tumors which belonged to the Borrmann type II led to an apparent cure, since the patient is still alive after 2½ years and without any sign of recurrence clinically, roentgenologically, and gastroscopically, but a patient having a grade 2 carcinoma which belonged to the Borrmann type IV had at the operation many lymph nodes, all of which exhibited carcinomatous invasion, and he died 2 years after the operation from recurrence. It is notable, furthermore, that so many type II carcinomas are found to be microscopically grade 4 tumors. If only the grade 1 and 2 tumors would give a good surgical prognosis, the outlook for sur-

gery of gastric carcinoma would be a dark one, since these tumors are so rare. But we feel that type II tumors belonging to grades 3 and 4 do not give a bad prognosis, do not develop early metastases, and may lead to satisfactory end-results. It should be stated that we have not yet seen a cure of a type III or IV carcinoma.



Fig 6 Microscopic section through the edge of the type II, grade 2 carcinoma described in Case 2. The perfectly sharp limitation of this carcinoma toward the surrounding gastric mucosa is well seen. Although this carcinoma involved the entire stomach total gastrectomy led to a 6 year cure.

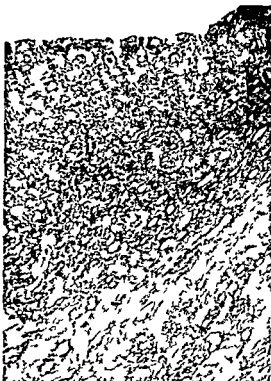


Fig 7 Microscopic section through type IV grade 4 carcinoma described. Ca 3 Th ct n sh th gre t st thick ss f the t m h h here m l m t r deep Alth gh th c ma was s lly m l l (8 by mm) the patient died 2 years 1 t f m r e

But it will not be contended that such a cure is never possible. It is obvious that the material presented is much too small to permit any definite conclusions. However, clinical course should not be confused with surgical cure. It may be that patients suffering from inoperable type IV carcinomas may live quite

TABLE I — COMPARISON BETWEEN MACROSCOPIC TYPES AND MICROSCOPIC GRADES IN 50 CASES OF GASTRIC CARCINOMA

Macroscopic	Microscopic			
	I	II	III	IV
Type I				3
Type II				5
Type III			3	5
Type IV				3
Total		5	6	3

some time—2 years or more—and that patients with resectable and curable type I and type II carcinomas may live only a short time if they are not operated upon at an early stage. It is our opinion that the retrospective analysis of the duration of a carcinoma until the death of its bearer does not permit any conclusion concerning the original surgical prognosis of the same case. It is the purpose of this paper to stimulate research about the relation of types of gastric carcinoma to the ultimate surgical prognosis. It seems to us possible that macroscopic diagnosis of types or histological examination—which however will have to be based on entirely new principles—may lead to the establishment of a surgical prognosis before the surgical interference.

### CONCLUSIONS

1. Classification of gastric carcinoma with consideration of its ultimate prognosis should be attempted.

2. Histological criteria according to the usual conceptions, especially grading, seem not to have a direct correlation to the gross appearance of gastric carcinoma to its clinical course or to its surgical curability. Therefore new attempts should be made to find histological criteria in better accordance with the factors.

3. Gross classification as suggested by Borrmann has proved to be satisfactory. Four gross types have been distinguished, the third and fourth of them may later be joined in a common group of infiltrative carcinomas. The first group is that of the circumscribed polypoid growth, the second that of the sharply limited non-infiltrating carcinomatous ulcer.

4. Histological grades and gross types of 50 gastric carcinomas have been compared and tabulated.

5. The preliminary impression that the gross types I and II often give excellent end results after surgical interference while the infiltrating types III and IV are unfavorable requires confirmation by extensive research.

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# THE PREVENTION OF POSTOPERATIVE PNEUMOCOCCUS (TYPE I) PNEUMONIA BY MEANS OF THE PROPHYLACTIC USE OF SULFAPYRIDINE

## An Experimental Study

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THE frequency with which the surgeon encounters postoperative pneumonia or pneumonitis in patients who are in poor preoperative condition has often suggested surgical delay. For similar reasons the surgeon and his medical confrere have indulged in procrastination in those instances in which the patient has an upper respiratory infection or is recovering therefrom. Even in those cases in which major surgical procedures are undertaken under more favorable physical conditions the morbidity from postoperative pneumonia creates an Acherontic problem in the management of the patient after surgical intervention. Coombs, in reviewing 3,894 operations, noted 13 lung complications with 11 deaths. In these 13 cases there were 8 instances of pneumonia with 7 fatalities. Lyons, in a study of 6,619 surgical cases, found 63 respiratory complications of which number 20 were due to pneumonia. In this latter group 23 terminated fatally. Roventine and Taylor studied 7,874 anesthetics. They noted pneumonia in 48 cases of which number 31 died. Cutler and Scott, in 41,368 surgical cases collected from the literature encountered 466 cases, 112 per cent of pneumonia of which number 215, 46.1 per cent died. It is often disheartening to the surgeon who performs a difficult operation with apparent success to see the patient succumb to postoperative pneumonia. Like many other conditions in medicine the malady has been recognized and reduced by various measures but still remains a potent factor in postoperative morbidity and mortality.

Since the successful introduction of chemotherapeutic agents in the treatment of pneumonia the question arose whether these same substances could not be used prophylactically in the prevention of postoperative pneumonia and if so employed whether they would cause any reactions which would contraindicate their use. Kolmer, in discussing the prophylactic value of such compounds states: "That the possibilities of the prophylactic value of sulfanilamide and its derivatives are worthy of careful attention is readily appreciated. But final appraisal must depend more on the results of carefully conducted animal experiments than on clinical observations because one cannot be sure in human beings that infection has or would have occurred. Certainly the compounds are rapidly absorbed and eliminated so that little or nothing is to be reasonably expected from single doses. In other words, prophylaxis demands the presence of effective concentrations in the blood over at least brief periods of time. But this can be readily attained and is probably of definite prophylactic value."

In this communication we propose to record our observations on the prophylactic use of sulfapyridine in the prevention of postoperative pneumococcus (type I) pneumonia in dogs; secondly to note the blood changes before, during and after the administration of sulfapyridine and to conclude therefrom whether any contraindications exist to the use of this chemotherapeutic agent in the prevention of postoperative pneumonia. In order to evaluate properly the results obtained in these experiments it was deemed advisable to subject each animal to the following three procedures allowing a 3 to 4 week interval

between stages (1) A simple abdominal laparotomy with manual manipulation of the viscera, (2) a simple gastrostomy in an animal premedicated with sulfapyridine and subjected postoperatively to an intrabronchial insufflation of a virulent culture of pneumococci, (3) an intrabronchial insufflation of a similar culture of pneumococci in an animal not premedicated with sulfapyridine

In this study 5 normal healthy dogs weighing between 18 and 28 pounds were used. The following blood studies were made during the experiments to be described: (a) oxygen content and carbon dioxide content of both arterial and venous whole blood, (b) determinations of hemoglobin, total red and white blood cells per cubic millimeter of blood, a differential white blood cell count and total sulfapyridine in those instances in which the drug was administered. These latter studies were performed on venous blood. In all cases the blood was taken from the femoral vessels and collected under oil. The oxygen and carbon dioxide values recorded represent the average of two determinations. The Van Slyke-Neill manometric method was employed for the oxygen and carbon dioxide determinations. Total sulfapyridine was determined by the Marshall and Litchfield method.

#### DETAILS OF EXPERIMENTAL PROCEDURE

Each animal received an intraperitoneal injection of a 10 per cent solution of sodium pentobarbital 30 minutes before operation, containing the equivalent of 0.1 grain of the salt per pound of body weight. The femoral vessels were exposed. In some instances the premedication was supplemented by local infiltration of a 1 per cent novocain solution before the vessels were exposed. Arterial and venous punctures were made to obtain blood for the studies. The animal was then anesthetized with cyclopropane and oxygen by a closed inhalation method. Water's to and fro carbon dioxide absorption technique was used. When the midsurgical stage of anesthesia (Guedel's classification) was reached and before the incision was made, arterial and venous blood samples were again removed from the femoral vessels. After 15 minutes of anesthesia, intervention was undertaken.

In the first part of this experiment a lower abdominal incision was made and the intestine was manipulated for about 5 minutes after which the wound was closed in layers. At the time the wound was being repaired, samples of arterial and venous blood were obtained. At the completion of the operation the animal was placed in a warm cage on its side. Arterial and venous blood samples were subsequently removed at intervals noted in the accompanying tables. The results of these blood studies are recorded in detail in part A of each protocol.

The second part of this experiment was performed 3 to 4 weeks after the previous stage, at the time when the animal had recovered completely. On the evening prior to surgical intervention, the femoral vessels were exposed under local anesthesia. Arterial and venous blood samples were obtained for the studies. A stomach tube was passed and an aqueous suspension of sulfapyridine containing 15 to 20 grains per pound body weight was introduced into the stomach via the tube. The following morning and about 3 hours before operation, this procedure was repeated. The animal then received the intraperitoneal injection of sodium pentobarbital and was anesthetized as described. The surgical procedure at this time consisted of a simple gastrostomy. Blood samples were taken at the same intervals as previously described. At the end of the operation 15 cubic centimeters of an 18 hour broth culture of pneumococcus type 1 was insufflated into a main bronchus under direct visualization of the bronchus. Approximately 100 cubic centimeters of air was used to spray the culture into the lung (Birnbaum's modification of the Coryllos-Birnbaum method). Following this procedure the animal was returned to a warm cage and placed on its side. At this time half the amount of sulfapyridine administered the night before operation was introduced into the stomach via the gastrostomy tube. Six hours after operation a similar dose was administered in the same manner. Beginning the following morning sulfapyridine was administered via the gastrostomy tube, every 6 hours for 3 days, the total daily dose was equivalent to the amount administered in the first pre-operative dose. Arterial and venous blood samples were ob-

tained at the same intervals as under the first part of this experiment. The results of these studies are recorded under part B of the protocols.

The third part of this experiment was performed 3 to 4 weeks after the second stage at a time when the animal had recovered completely. The same procedure was followed as in part B except that no sulfapyridine was administered and no operation was performed. The animal received an intraperitoneal injection of sodium pentobarbital and then was anesthetized with cyclopropane and oxygen. After 20 minutes of inhalation anesthesia the culture of pneumococci was sprayed into a main bronchus. The animal was then returned to a warm cage. Arterial and venous blood samples were taken before the anesthetic was administered during and after anesthesia. The results of these studies and the additional blood determinations in this part of our study are recorded in part C of the protocols.

In addition each animal was studied roentgenographically before and after each surgical procedure. The findings in these studies are also presented in the protocols.

Since our conclusions as to any contraindications to the prophylactic use of sulfapyridine will be based chiefly upon the changes in the blood accompanying the administration of sodium pentobarbital, cyclopropane and sulfapyridine, it would not be amiss to present a brief review of the changes even in normal animals under the influence of these medications.

**Normal blood constituents and gases.** Morris, Stelton, Allison and Green in a comprehensive study of the normal blood constituents in the adult dog conclude that there are 6.2 million red blood cells per cubic millimeter and 13.2 grams of hemoglobin per 100 cubic centimeters of blood. The total white blood cells is estimated at 11,467 per cubic millimeter with a differential white count of 71.8 polymorphonuclear neutrophils, 21.7 lymphocytes, 5.4 eosinophils and less than 1 monocyte per 100 white blood cells.

Regarding the normal blood gases, Campbell and Poulton (3) state that arterial blood contains about 20 cubic centimeters of oxygen per 100 cubic centimeters of blood while

venous blood contains 13 to 15 cubic centimeters. The normal oxygen content of arterial blood being about 95 per cent of its total oxygen carrying capacity. These authors also state that the arterial carbon dioxide content is 52 cubic centimeters per 100 cubic centimeters of blood whereas the venous carbon dioxide is 58 cubic centimeters. In a study of the arterial and venous oxygen and carbon dioxide content in 15 resting patients, Harrop concludes that the oxygen content of arterial blood varies between 13.9 and 24.1 volumes per cent whereas the venous oxygen content varies from 10.5 to 17.6 volumes per cent. The carbon dioxide content of the arterial blood ranges from 44.6 to 54.7 volumes per cent, the venous being between 48.3 and 60.4 volumes per cent. Harrop gives the following figures as the limits of oxygen and carbon dioxide content of artery and vein<sup>4</sup>:

#### LIMITS OF ARTERY AND VEIN CONTENT

O <sub>2</sub> %	CO <sub>2</sub> %	O <sub>2</sub> %	CO <sub>2</sub> %
Arterial	Venous	Arterial	Venous
13.89	17.77	48.3	52.8
21.3	15.81	50.55	58.74
5.31	1.5	5.89	55.88
23.04	17.61	5.76	57.5
2.0	3.3	44.38	5.00
1.9	4.6	54.69	56.71
17.75	0.9	44.84	45.27
7.87	3.94	5.3	60.41

#### Changes induced by sodium pentobarbital

Tatum, reviewing the subject of barbiturate medication, states that in moderate doses there is little effect upon the blood constituents. At times however it will cause splenic engorgement with a resultant dilution of the circulating blood. This will produce a decrease in the red blood cell and a proportional increase in the white blood cells of the circulating blood. Siebert and Thurston have noted no significant changes in oxygen consumption in those cases in which small doses of barbiturates were employed. Under larger doses of the same drug it is sufficient to produce corneal anesthesia. Shapiro observed a profound lowering of the oxygen consumption. From these studies it would therefore appear that the lowering of oxygen consumption is

<sup>4</sup> The total volume of blood in the body is about 5 liters. The volume of blood in the heart is about 1 liter. The volume of blood in the lungs is about 1 liter. The volume of blood in the rest of the body is about 3 liters. The volume of blood in the arteries is about 1 liter. The volume of blood in the veins is about 1 liter. The volume of blood in the capillaries is about 1 liter. The volume of blood in the interstitial spaces is about 1 liter. The volume of blood in the lymphatic system is about 1 liter. The volume of blood in the digestive system is about 1 liter. The volume of blood in the respiratory system is about 1 liter. The volume of blood in the circulatory system is about 1 liter. The volume of blood in the body is about 5 liters.

proportional to the dosage of barbiturate. In moderate dosage of the drug the carbon dioxide capacity and content shows some degree of increase (22). This is due in all probability, to the alkalininity induced by the soluble barbiturate. If on the other hand large doses are used, sufficient to cause respiratory depression, an acidosis may be produced with a resultant increase in the carbon dioxide content of the blood.

*Changes induced by cyclopropane* Taylor and Waters (29) have shown that a leucocytosis takes place following cyclopropane anesthesia which is essentially the same as that of any other anesthetic agent. The total number of white bloodcells following an abdominal surgical exercise (under cyclopropane anesthesia) may rise from normal to about 25,000 per cubic millimeter. The increase in cells is chiefly in the polymorphonuclear leucocytes—rising from 60 per cent to approximately 90 per cent. The maximum rise is effected in 8 hours and does not return to normal for 2 or 3 days. This opinion is shared by Waters and Schmidt (34), who further add that "erythrocyte counts have been made before, during, and after cyclopropane anesthesia. Little change in the number of red blood cells was noted."

Waters (33), in presenting an analysis of arterial and venous blood gases before and during cyclopropane and oxygen anesthesia, observes that during anesthesia the concentration of oxygen in the veins is almost as great as within the arteries. Robbins and Baxter, studying arterial oxygen and carbon dioxide in 9 dogs, noted that while the animal was awake the average arterial oxygen content was 18.2 volumes per cent and the carbon dioxide content was 40.5 volumes per cent. These same animals under cyclopropane and oxygen anesthesia showed an oxygen content of 20.6 volumes per cent and a carbon dioxide content of 42.7. When the anesthetic was deepened to the stage of respiratory arrest, the carbon dioxide rose to 52.1 and the oxygen fell to 15.2 volumes per cent.

*Changes induced by sulfapyridine* Toomey, Reichle, and Takacs studied the effects of 10 grams of sulfapyridine upon the blood constituents of normal monkeys weighing ap-

proximately 3 kilograms. They conclude that "the M. Malatta monkeys showed a decrease in the total number of red blood cells and their hemoglobin content, an increase in the total number of white blood cells and occasionally a reversal of the leucocyte-lymphocyte ratio." Machella and Higgins after studying the effects upon the erythrocyte count conclude that "at the end of 1 week (of administration of 1 gram of sulfapyridine per kilogram body weight) there was no change in the erythrocyte count but at the end of the second week the mean number of erythrocytes was below that observed during the control period."

A careful search of the literature fails to reveal any reference to the oxygen, carbon dioxide arterial and venous changes during sulfapyridine therapy. Regarding the presence of reduced hemoglobin in the circulating blood Vigness, Watson, and Spink state that "It is of interest that over 50 patients have been observed while being treated with sulfapyridine. In but 1 of these patients has cyanosis been noted following sulfapyridine therapy." Campbell and Morgan (2), however, believe it to be more common, and in a study of 32 cases of pneumonia treated with sulfapyridine call attention to the presence of methemoglobin in 25 cases. This, however, does not imply that the oxygen carrying power of the blood was sufficiently reduced to produce cyanosis. Regarding the development of cyanosis, it is interesting to add the opinion of Long and Bliss. They state "it does not seem to be common in the course of sulfapyridine therapy." In our experience cyanosis has not been an alarming toxic manifestation and can generally be disregarded."

## PROTOCOLS

### Animal 1

*Part A* A male hound weighing 27½ pounds was subjected to the three procedures which have been described. Following the first part the postoperative course was uneventful. Blood studies made during this part of the experiment showed the changes shown in Table I, Part A.

*Part B* On the twenty-first day after operation the second part of this study was performed. For the first 2 days after operation the animal ate poorly but was otherwise well. On the morning of the third day the gastrostomy tube was removed. From that

TABLE I—BLOOD STUDIES ON ANIMAL 1 PART A

	O <sub>2</sub>		C bo d r l		Blood t					
	Arter l	V ou	Arter l	V ou	Hgb	RBC	WBC	P	L	E
P-operat	6	7.9	5	5	5	5	8	6		8
Du g es hes	4	9.7	45.7	3.8						
E d f es b	8.5		5.9	5.6						
Half h post pe	4.4	7.7	44	5.7						
4 hours post pe	7		45.4	5.3	6	8	6.8	6	35	5
1 d y postoper ti	5.3	7	5.7	5.8	8	8	4	6	3	3
nd d y postoper	5.4	7.7	48	5.7	4.6	8	8.8	7	5	
3 d day post pe	5.3	17.5	43.9	40.6	4.8	5		7	7	
4th day po-oper t	5	5	54	40.8	8	4.8	7.8	75		
5 h d y post pera ve	8			3	1.8	8	1.8	65	5	

O<sub>2</sub>—If dea bo dioxid al re p essed i volumes pe eante t  
 Hgb—If m glob in g m p t  
 RBC—T tal urebe (m l) f ed blood fls pe cub m l/m  
 WBC—T eo polym rph  
 P—t lymphocy es  
 E—t eos ph l  
 S—T l l py d ia m l/gram p ent

TABLE I—PART B

	O <sub>2</sub>		C bo d nd		Blood t						S
	Ar t	V ou	Ar t l	V ou	Hgb	RBC	WBC	P	L	E	
P per t	6.8	4	4	5.5	4	4.4	8	60	3	5	8
Duri g nesthes	8	3	44	3.7							
E d f es hes	8.6	6	45	5							
Half hour postoperati	7	3.9	4.8	35.5							8
h ous pos operat	7	6	5		3.8		8		35	5	8.7
1 d y pos pe	6	8	7	3.6	3.8		5.8	6	30		8
nd d pos pe	3.9		8	35	3.6	3.8	5.6	5			8
d da pos ope	6.8	3.4	3.5	5	8	3.8	5.8	55			7.8
4th d pos pera	6	7	3	3			6	5	40		6
5 h d y pos per ve	6		8	3	3		8	6	7		6

TABLE I—PART C

	O <sub>2</sub>		Carbo d d		Blood t					
	Art rial	V ou	Art rial	V	H b	RBC	WBC	P	L	E
Pre-operat ve	7.5		6	5.6	6	8		65		5
Du ng nesthesia	9	3.8		53						
End f anesthes		5.3		5						
Half hour pos opera	3		7	55.8						
h rs postopera	6.5	8	3	5			9	7	5	
day pos opera	6	9	5	55.7	8	4		3	5	
nd da pos opera	7	8.9	5	55			6	70		
d day pe per		8	40.6		4.6			80		

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day on the animal ate better and moved about in a perfectly normal manner. X-ray studies of the chest made daily for the first 5 days after operation showed no abnormal findings. Blood studies made at regular intervals showed the changes indicated in Table I, Part B.

*Part C* Four weeks later, the third part of this study was undertaken. On the evening of the day of operation the temperature rose to 104.4 degrees F and the dog appeared sick. The animal refused to eat, drank very little, and did not move about. The respirations were rapid and shallow. On the third day after operation the animal died. Daily x-ray studies of the chest showed an advancing right sided pneumonia. Necropsy performed on the day of death revealed pneumonia of the lower two lobes on the right side. Blood studies made during this part of the experiment are recorded in Table I, Part C.

## Animal 2

*Part A* A male poodle weighing 25½ pounds was subjected to the procedures described. Following the first part of this experiment the animal's recovery

was rapid with an uneventful postoperative course. Blood studies made during this phase of the experiment showed the changes indicated in Table II, Part A.

*Part B* Twenty six days later, the second part of this experiment was performed. On the evening of the day of operation the temperature rose to 103.6 degrees. Roentgenographic examination of the chest 8 hours after the operation showed an infiltration of the right lung corresponding to the medial part of the right middle lobe. On the morning of the first day after operation the temperature was 101.6 degrees. An x-ray study of the chest made 24 hours after surgical intervention showed no further advancement of the lesion, and on the next day there was complete resolution of the infiltration. The postoperative course thereafter was uneventful. The sulfapyridine was discontinued on the evening of the third day after operation and the gastrostomy tube was removed the following morning. X-ray studies of the thorax made after the second day following operation showed no changes suggestive of residual pneumonic infiltration. Blood studies made during

TABLE II—BLOOD STUDIES ON ANIMAL 2, PART A

TABLE II —BLOOD STUDIES ON ANIMAL 2, 11										
	Oxygen		Carbon dioxide		Blood constituents					
	Arterial	Venous	Arterial	Venous	Hgb	RBC	WBC	P	L	E
	16 9	13 2	47 1	48 1	12 8	5 0	13 2	60	34	0
Pre operative	17 8	13 7	42 9	48 6						
During anesthesia	18 4	14 9	43 7	54 6						
End of anesthesia	16 7	14 1	41 8	51 2						5
Half hour postoperative	16 7	13 0	39 3	52 2	12 4	4 8	14 2	70	25	4
4 hours postoperative	15 7	12 3	41 1	49 9	12 6	4 8	18 4	72	24	3
1st day postoperative	16 1	12 4	40 3	49 7	1 8	5 0	18 0	74	23	3
2nd day postoperative	15 5	13 7	40 7	47 2	12 8	5 0	16 8	74	25	4
3rd day postoperative	15 9	13 0	42 8	48 1	12 4	4 6	17 2	70	26	5
4th day postoperative	16 3	13 6	41 6	47 6	1 4	4 8	17 0	71	24	
5th day postoperative										

TABLE II —PART B						
	Carbon dioxide	Blood constituents				S
		RBC	P	L	E	

TABLE II—PART B

TABLE II—PART B											
	Oxygen		Carbon dioxide		Blood constituents						S
	Arterial	Venous	Arterial	Venous	Hgb	RBC	WBC	P	L	E	
					13 0	4 8	17 9	53	40	6	
Pre operative	18 0	15 1	41 3	49							6 6
During anesthesia	18 0	15 1	43 4	51 6							
End of anesthesia	18 0	15 1	44 7	54 2							7 2
Half hour postoperative	18 0	15 1	44 0	53 8							7 9
4 hours postoperative	18 0	15 1	41 7	51 6							8 7
1st day postoperative	17 1	15 4	43 7	50 8	1 6	4 8	17 0	55	39	6	8 7
2nd day postoperative	17 9	14 7	41 8	48 6	1 0	4	16 2	54	41	5	8 7
3rd day postoperative	18 4	13 9	44 6	50 5	12 0	4 2	15 8	53	43	4	9 7
4th day postoperative	17 5	14 1	4	0 0	11 5	4 0	15 0	51	45	4	7 7
5th day postoperative	17 1	14 1	4 8	49 9	12 0	4 2	16 2	66	31	3	4 4

TABLE II—PART C

	Oxygen		Carbon dioxide		Blood studies					
	Arterial	Venous	Arterial	Venous	Hgb	RBC	WBC	P	L	E
Pre-operative	54	3	4	47.3	6	6		63	3	6
During anesthesia	3	5	43.3	9.9						
End tracheal tube		6	4.8	55						
Half hour postoperative	7		5	54.8						
4 hour postoperative	5.5	4	47.3	55		4.4	8	75	3	
1 day postoperative	3	6.9	6.7	54.7		4		79		
2 day postoperative	9.8	6.3	48.9	55.5	6	3.8	6	8	8	
3rd day postoperative	8	5	7	60.8	8	8	3	81		

this part of the experiment are recorded in Table II Part B

**Part C** Thirty days after part B the third part of this study was performed. Four hours after institution of the culture into the bronchus the animal had a chill and the temperature dropped to 96 degrees F. X-ray study of the lungs showed a suspicious infiltration of the right lower lobe. The following day the animal was quite sick, breathing rapidly, drooling at the mouth and unable to walk about. The temperature rose to 103.8 degrees. X-ray studies of the chest at this time showed a patchy pneumonia involving the greater part of the right lung. On the morning of the fourth day after operation the animal died. X-ray study of the lungs made on the third day after operation showed a massive consolidation of the right lung. Necropsy on the fourth day after operation revealed a massive consolidation of the right lung with a patchy pneumonia of the left lung. Blood studies made during this part of the experiment are recorded in Table II Part C.

#### Animal 3

**Part A** A mongrel dog weighing 18 pounds was subjected to the three procedures which have been

described. Following this part of the experiment the animal's recovery was immediate and the postoperative course was uneventful. The control blood studies made in this part of the study showed the changes indicated in Table III Part A.

**Part B** On the twenty-seventh day after operation the second part of this experiment was performed. Whereas in the previous experiments the animal was prepared with sulfapyridine the night before the operation as well as on the morning of the operation, the former dose was omitted in this case. On the first day after operation the animal appeared fatigued but otherwise quite well. X-ray examination of the chest at this time showed no abnormal changes within the lungs. On the second day after operation the animal appeared brighter and from then on the recovery was uneventful. Repeated daily x-ray studies for the next 4 days showed no changes which could be interpreted as pneumonitis. On the morning of the fourth day after operation the administration of sulfapyridine was discontinued and the gastrostomy tube was removed the following morning. Blood studies made at regular intervals during this phase of the experiment are recorded in Table III Part B.

TABLE III—BLOOD STUDIES ON ANIMAL 3 PART A

	Oxygen		Carbon dioxide		Blood counts					
	Arterial	Venous	Arterial	Venous	Hgb	RBC	WBC	P	L	E
Pre-op	6			4	3			6		7
During anesthesia										
End tracheal tube		3		50						
11 hours postoperative	6		5	5						
4 hours postoperative	5		5.8	5			8	60	3	
1 day postoperative	6	3	43.3	5		8		68		
2 day postoperative	6	5	8	9	3	8	8	5	3	
3rd day postoperative	5		4		8	8	6	7		
4th day postoperative	6			48.8	8			3		3
5th day postoperative	6	5	6			6	5	7	8	

TABLE III—PART B

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TABLE III—PART B

	Oxygen		Carbon dioxide		Blood constituents						S
	Arterial	Venous	Arterial	Venous	Hgb	RBC	WBC	P	L	E	
Pre-operative	16 3	11 9	42 2	49 1	12 8	4 8	12 2	58	35	7	5 5
During anesthesia	16 9	13 2	41 9	50 2							
End of anesthesia	17 8	15 0	43 5	54 3							
Half hour postoperative	16 7	12 9	41 6	57 8							6 1
4 hours postoperative	16 3	11 6	41 9	50 7	12 6	4 6	17 0	57	38	5	7 2
1st day postoperative	15 9	10 9	40 8	48 6	12 2	4 4	17 8	53	45	2	8 9
2nd day postoperative	15 4	11 2	41 4	50 8	12 0	4 0	17 6	51	48	1	8 5
3rd day postoperative	15 8	11 5	42 8	51 1	11 8	3 8	18 4	64	34	2	8 7
4th day postoperative	16 7	10 9	42 6	50 0	12 0	4 0	18 0	76	23	1	6 6
5th day postoperative	16 9	11 0	41 1	47 7	12 4	4 4	17 2	77	23		4 2

TABLE III—PART C

	Blood constituents				S
	WBC	P	L	E	
Pre-operative	12 2	58	35	7	5 5
During anesthesia					
End of anesthesia					
Half hour postoperative					
4 hours postoperative	17 0	57	38	5	6 1
1st day postoperative	17 8	53	45	2	7 2
2nd day postoperative	17 6	51	48	1	8 9
3rd day postoperative	18 4	64	34	2	8 5
4th day postoperative	18 0	76	23	1	8 7
5th day postoperative	17 2	77	23		6 6

TABLE III—PART C

TABLE III—PART C										
	Oxygen		Carbon dioxide		Blood constituents					
	Arterial	Venous	Arterial	Venous	Hgb	RBC	WBC	P	L	E
Pre-operative	13 9	10 8	41 6	49 2	13 4	4 5	12 0	6	30	8
During anesthesia	16 2	12 6	40 2	51 4						
End of anesthesia	16 7	13 8	42 3	53 2						
Half hour postoperative	15 6	10 1	40 1	49 6						6
4 hours postoperative	11 1	9 7	44 7	53 2	13 0	4 3	20 0	70	24	2
1st day postoperative	9 8	7 2	45 8	54 2	12 8	4 4	28 0	76	24	2
2nd day postoperative	5 6	4 8	48 6	57 6			34 0	84	14	

after operation, the dog was quieter than usual, however, he ate and drank fairly well. From then on was up and about as heretofore. The sulfapyridine discontinued on the evening of the third day. The gastrostomy tube was removed on the morning of the fifth day.

*Part C* Twenty-eight days after the second operation was done, the third part of this experiment was performed. During the first few hours after anesthesia the animal appeared very much like that after the second procedure. However, after the fourth hour following operation he appeared acutely sick, drooled at the mouth, refused all food, and drank very little. The animal's breathing was rapid. On the evening of the second day after operation the dog was found dead in the cage. Periodic x-ray studies made after the fourth hour after operation showed a pneumonia on the left side which progressed to involve the entire lung and part of the right lung. Postmortem examination showed a massive consolidation of the left lung with involvement of the right middle and lower lobes as well. Blood studies made during this phase of the experiment are recorded in Table III, Part C.

#### Animal 4

*Part 1* This dog was a female chow weighing 19 pounds. Following surgical intervention the postoperative course was uneventful except for a low grade wound infection. Blood studies made during this experiment are recorded in Table IV, Part A.

*Part B* Twenty-one days later the second part of this study was undertaken. For the first 24 hours

after operation, the dog was quieter than usual, however, he ate and drank fairly well. From then on he was up and about as heretofore. The sulfapyridine was discontinued on the evening of the third day after operation, the gastrostomy tube was removed on the fourth day and on the evening of the fifth day the animal was sacrificed. X-ray studies made daily showed no changes within the lungs which could be interpreted as pneumonia. At autopsy the lungs were found to be normal throughout. Blood studies made during this part of the experiment are recorded in Table IV, Part B.

#### Animal 5

*Part A* A mongrel male dog weighing 23½ pounds was operated upon as described heretofore in this part of our study. The postoperative course was uneventful. Blood studies made during this part of the experiment are recorded in Table V, Part A.

*Part B* Twenty-four days after the first operation was performed, the second part of this experiment was undertaken. Within the first 6 hours after operation the animal was up and about, quite active, and perfectly normal in behavior. On the evening of the third day after operation the sulfapyridine was discontinued and on the fourth day the gastrostomy tube was removed. That evening there was an evis-



TABLE IV—BLOOD STUDIES ON ANIMAL 4 PART A

	Oxy		Carbo dioxide		Blood counts					
	Arterial	Venous	Arterial	Venous	Hgb	RBC	WBC	P	L	E
Pre-operative	6	3		5.2	6	8	8	5	37	
During anesthesia	5.9	4	3	9						
End of anesthesia	8	3	9	5						
Half hour postoperative	6	6	4	5.9						
1 hour postoperative	6	8		47.3	3.6	6	7	60		7
2 hours postoperative	5.9	9		48	3.6	4.8	8.5	65	3	5
3 hours postoperative	6.4		4.7	9	3	6	9.4	7	7	
4 hours postoperative	6	3		6.6	3.3	8	8	7	6	
5 hours postoperative	6	7	4	7	3.6	4.6	6.4	7	3	
6 hours postoperative	6.7		3	47	3	6	6	7		

TABLE IV—PART B

	Oxy		Carbon dioxide		Blood count						S
	Arterial	Venous	Arterial	Venous	Hgb	RBC	WBC	P	L	E	
Pre-operative	6.9		9	3.8	3	6		58	37	5	7
During anesthesia	7.8	7	43.6								
End of anesthesia	8.8		44	3.8							
Half hour postoperative			4	3.6							8.3
1 hour postoperative	6.7		7	3.8	3	4	7	57			8
2 hours postoperative		9	45.3	5			7	30			8.6
3 hours postoperative	9	9.8	3.8	47.9	3		6.8	3	44		
4 hours postoperative	5.7	8		3.6	8	3.8	6	56	3		
5 hours postoperative	6		5		8		3.6	6		3	5
6 hours postoperative				8.8			3	6			

ceration of the intestines and the animal died. X-ray studies made daily after the operation showed no pulmonary infiltration suggestive of pneumonia. An autopsy performed the same day as the eviceration

revealed perfectly normal lungs and no areas suggestive of pneumonia. Blood studies made during the part of the experiment are recorded in Table V, Part B.

TABLE V—BLOOD STUDIES ON ANIMAL 5 PART A

	Oxy		Carbon dioxide		Blood counts					
	Arterial	Venous	Arterial	Venous	Hgb	RBC	WBC	P	L	E
Pre-operative	8		36.8		8			6	3	3
During anesthesia	9	6		7.8						
End of anesthesia				5						
1 hour postoperative	3	6		6.9						
2 hours postoperative	6.7		30.8	8	6	4.6	3	8	9	
3 hours postoperative			6		6	6				
4 hours postoperative	6.3		6.6		8	3	3.6	3	7	
5 hours postoperative					6	8	5			
6 hours postoperative		9	30.8	3	6	6		70	3	
7 hours postoperative	6	8		44	6	6	6	66	3	

TABLE V—PART B

	Oxygen		Carbon dioxide		Blood constituents					S
	Arterial	Venous	Arterial	Venous	Hgb	RBC	WBC	P	L	
					12.8	4.6	10.8	58	37	4.1
Pre-operative	15.0	13.9	38.5	42.9						5.9
During anesthesia	20.8	17.3	39.2	45.7						6.2
End of anesthesia	21.4	16.4	41.8	46.9						8.1
Half hour postoperative	17.3	13.0	40.2	43.2						7.6
4 hours postoperative	18.2	14.4	41.8	47.1	12.4	4.4	15.8	62	35	8.1
1st day postoperative	17.7	12.6	40.2	47.1	12.2	4.2	15.4	60	38	8.8
2nd day postoperative	16.9	10.2	39.6	46.1	12.0	4.0	16.0	57	40	4.1
3rd day postoperative	16.6	13.0	38.9	44.6	11.8	3.8	16.0	61	38	4.1
4th day postoperative	17.1	17.7	38.7	44.3	11.8	3.8	18.0	67	37	4.1

## EVALUATION

Following the introduction of the sulfonamides as curative agents in the treatment of infection, it was a natural sequence of events that an attempt be made to employ them prophylactically. Although there are many different opinions as to the mechanism of bacterostatic action of these drugs, all seem to agree that in adequate doses the effectiveness of the sulfonamides is based upon their ability to limit bacterial multiplication. Woods, in a study on the modus operandi of sulfanilamide, concludes that bacteriostasis is based upon inhibition of enzyme reaction involved in the utilization of p-aminobenzoic acid essential for bacterial growth. In reviewing the literature on the prophylactic use of sulfapyridine in the prevention of experimental pneumonia, we note that Gregg, Loosh, and Hamburger report unfavorable results in the dog. They state that "lobar pneumonia can evolve despite the administration of large doses of sulfapyridine before and after infection and despite its presence in the blood in concentrations equal to or greater than those obtaining under conditions when the drug is regularly curative." Goldstein and Graef (9), in a similar study in rats, show a close agreement with the findings of Gregg, Loosh, and Hamburger. Goldstein (8) adds that, while the lungs may have shown pneumonia at autopsy, it was difficult to state conclusively that the animals had clinical pneumonia.

A casual examination of the methods employed by Gregg, Hamburger, and Loosh (10) and of those presented in this communication

fails to reveal any remarkable differences in experimental procedure. Yet, the final results are not in agreement. Whereas we were unable to produce pneumonia in all but 1 of our dogs after the prophylactic use of sulfapyridine, they were able to induce pneumonia in each of 6 dogs. A more careful study of their methods, protocols, and final results reveals some important differences in the details of experimental procedure—particularly as it pertains to the use of sulfapyridine and the course of the pneumonic process. Table VI is a résumé of the sulfapyridine blood concentrations and quantity of drug administered by Gregg, Hamburger, and Loosh.

Before infection was produced by these latter authors, sulfapyridine was given in two divided doses. The first dose was administered 18 to 24 hours before infection was induced and the second 6 to 12 hours before infection. After infection sulfapyridine was given again in 2 divided doses. The first was given 6 hours and the second 12 to 18 hours after infection. It will be noted that an interval of at least 12 to 18 hours had elapsed between the last dose before the pneumococci were instilled into the bronchi and after its introduction. Since all animals were sacrificed 24 hours after infection, it is assumed that the sulfapyridine blood levels presented in Table VI are those of blood taken shortly before the animals were sacrificed. Reference to this table shows a rather high sulfapyridine blood level before the infection was produced and a marked drop before the animal was sacrificed. It seems difficult to reconcile these data with the results

TABLE VI—RÉSUMÉ OF CONCENTRATION IN EXPERIMENTS OF GREGG HAMBURGER AND LOOSLI

Dog	Concentration of drug in blood in milligram per cc		Quantity of drug administered in grams	
	Before infection	After infection	Before infection	After infection
S T		8	5	
S T	4	3.7	4	4
T	3.3	1.6		
S T	8	8	3	
S T		5		4
S T	8	5	4	4

reported by other investigators. In most instances the reports indicate a rise in the sulfapyridine blood level during the administration of the drug until a constant is reached and then a decline after its discontinuance—but not quite as sharp a drop as portrayed in Table VI. In our cases after the drug was discontinued the blood level dropped slowly and 36 hours after the last dose was administered there was still present a fair concentration within the blood stream. Even Gregg Hamburger and Loosli in other parts of their study find that such sudden decline in blood level is the exception rather than the rule. Perhaps one of the reasons for the difference in final results is the long interval between the pre-infection and postinfection dosages of the sulfapyridine. The lower blood level recorded by Gregg Hamburger and Loosli after infection was induced may imply either a failure to receive, absorb or utilize the drug while elimination continued at a normal rate.

Further since these authors sacrificed all animals 24 hours after infection was induced they were therefore unable to draw any conclusions as to the course and eventual outcome of the disease in these 6 dogs. In our cases daily x-ray studies of the lungs (in those animals receiving sulfapyridine prophylactically) failed to show postoperative pneumonia in all but 1 case. In this instance there was complete regression of the lesion (on the subsequent roentgenograms) 48 hours after infection was induced. In the animals reported in this communication receiving sulfapyridine prophylactically and sacrificed on the fourth and fifth day after infection there was no

roentgenographic or necropsy evidence of pneumonia. In the autopsy studies on rats sacrificed at 24 hour intervals Gold ten and Graef observed that in the treated animals there was no progress of the lesion in the lungs after the first 24 hours. The lesion remained a sharply localized process and thus provided a contrast with the spreading infection which so consistently characterized the controls. After the first 24 hours these authors also noted that the pneumonic process in the treated group of cases was abacterial. Gregg Hamburger and Loosli also state that the potential efficacy of sulfapyridine as a life saving therapeutic agent in pneumococcal infection is especially evident in the recovery of certain of the dogs showing a well advanced disease by the end of 18 to 24 hours when treatment was begun. In several of these instances the findings were such as to indicate a high probability of fatal termination. That it is able to promote an arrest of infection is also shown by the brevity of the febrile stage, the restricted size of the pulmonary lesion and the limited occurrence of bacteremia in dogs treated earlier in the disease. Thus implying an inhibitory effect of sulfapyridine on the pneumonia. If the bacteriostatic action of sulfapyridine is based upon the presence of effective concentrations within the blood then it appears logical to expect that if the drug is present in the blood (at that concentration) and pneumonia does develop the course should be benign and the mortality diminished.

Recently Hinshaw and Moersch have employed sulfapyridine in the treatment of 21 cases of postoperative pneumonia. They state that the maximum temperature of nearly half of the patients approached normal within 24 hours after the beginning of treatment with sulfapyridine. The condition of most of the remainder was significantly improved in 48 to 72 hours. The results were similar whether or not pneumococci were found in the sputum. Postoperative pneumonia responded as well as primary pneumonia. Older patients responded as well as younger ones. Only 1 death occurred. This was a case of early fulminating postoperative pneumonia which developed on the second day after extraperitoneal resection of a carcinoma of the colon. It

is of interest to note that Lockwood and Ravdin using sulfanilamide prophylactically (to prevent peritonitis) in 22 cases of colon resection and in 6 cases of inflammatory or traumatic perforation of the intestinal tract did not encounter a single case of postoperative pulmonary infection. Garlock and Seley in 21 cases of colon resection, using sulfanilamide in the same manner encountered but 1 instance of postoperative pulmonary infection. This was a case of fulminating tracheobronchitis with bronchopneumonia of the influenzal type. From the foregoing, it therefore appears that the sulfonamides may be used both as curative and prophylactic agents in postoperative pneumonia.

In an analysis of the hematological and blood gas studies, we have noted no apparent contraindication to the use of sulfapyridine in the prophylaxis of postoperative pneumonia. The results of this part of the study may best be appreciated when presented in table and graphic form. In the tables presented in the protocols it will be noted—in part A of each study—that the preoperative blood constituents were those of normal dogs and that the postoperative reaction was essentially that of a normal dog except that the total white blood cells did not rise quite as high as in the cases of Taylor and Waters, that the normal level was attained on the fifth day after operation and that the number of polymorphonuclear neutrophils did not rise quite as high as in their cases. In part B of this experiment, i.e., the animal being given sulfapyridine before operation and receiving postoperative insufflation of pneumococci into the bronchus, we note that the rise in white blood cells is not quite as high as in the previous part of this study. Further, that the maximum elevation in white blood cells occurs a day or two later than in the first part of the investigation and that after 5 postoperative days the total number of white blood cells is at a higher level than in those instances in which the animal was not given sulfapyridine. In the white blood cell differential study we also note that the number of polymorphonuclear leucocytes does not rise quite as high as in those instances in which the animal did not receive sulfapyridine. The red blood cells and hemoglobin show but slight

difference in the two parts of this study. There is, however, a tendency for a longer sustained drop in these blood constituents under sulfapyridine than in those instances in which the animal was not given sulfapyridine. In the third part of this study, i.e., in which the animal received an intrabronchial insufflation of pneumococci but was not given sulfapyridine, the blood picture is that of the typical bronchopneumonia. In these instances there was a rapid rise in the white blood cells, an increase in the polymorphonuclear neutrophils and a fall in the hemoglobin and red blood cells. From the data presented it may therefore be concluded that, in the experimental animal, the blood constituent changes following the prophylactic use of sulfapyridine are not very different from those seen in the animals having a smooth and uneventful postoperative course.

The final chapter of this study concerns itself with the changes in the blood gases. The results of this part of the investigation can best be appreciated when presented in graphic form (Figs 1 to 5). By reference to these graphs it will be seen that during anesthesia (in all three parts of this study) the arterial and venous blood oxygen content<sup>1</sup> may increase. The amount of increase, however, varies with each animal and evidently with the amount of oxygen made available to it during the anesthetic. The carbon dioxide too may increase. These blood reactions are similar to those described by Waters and by Robbins and Baxter. Soon after the anesthetic is discontinued there is a decline in the blood gas content, and in the normal animal the preoperative level is attained in about 4 hours. Under sulfapyridine therapy the arterial oxygen content is essentially the same as in the normal animal—showing no interference with oxygen intake. The venous oxygen, however, falls to a lower level and does not return to normal for another

<sup>1</sup>We have chosen to report the arterial and venous blood oxygen content rather than the capacity, because the former tells us the actual amount of oxygen present in the circulatory system and available to the tissues while the latter merely implies a potential oxygen carrying power of the blood. A reduction in the content sufficient to produce asphyxia need not necessarily be followed by a corresponding reduction in the oxygen capacity of the blood. Stadie in a study on oxygen capacities in pneumonia remarks that "no unusually low total oxygen capacities were observed even in fatal cases with intense cyanosis. On the contrary, in these cases the total oxygen capacity was unusually high, pointing toward a concentration of blood. Again, in only one case was there any marked fall in the oxygen capacity during the illness."

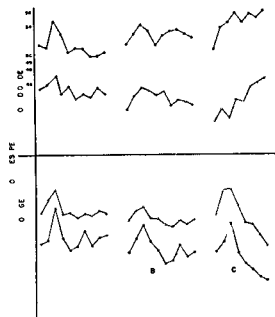


Fig Animal

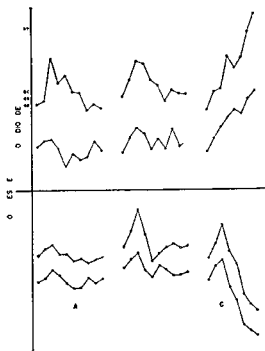


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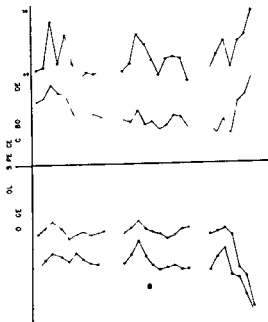


Fig 3 Animal 13

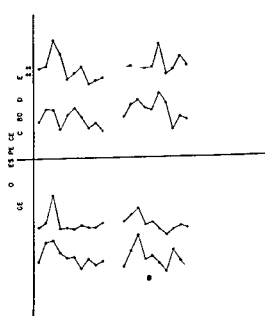


Fig 4 Animal 4

(Fig 4 opposite page)

day—implying a greater need and utilization of oxygen during the first day. The carbon dioxide—in the cases receiving sulfapyridine—in both artery and vein tends to remain elevated for the first 24 hours after operation. At no time, however, is there an abnormally low oxygen supply, excessive utilization of oxygen, or an accumulation of carbon dioxide in the blood to be out of proportion with that seen after cyclopropane anesthesia itself. It is interesting to observe the blood gas changes taking place in the animals developing pneumonia. Here the arterial and venous blood oxygen content diminishes progressively so that the arterial blood contains less oxygen than normal venous blood. At the same time the carbon dioxide in the veins and arteries rises steadily. Meakins and Davies, in a study of the arterial blood gases in cases of bronchopneumonia, state "It will be noted that in all those cases where the arterial oxygen saturation and carbon dioxide content were estimated, there was a parallelism between oxygen desaturation and the carbon dioxide content of the arterial blood—the greater the former, the greater the latter."

The sulfapyridine blood levels after the administration of that agent are presented in the protocols. The concentrations before operation varied between 4.1 and 8.2 milligrams per cent; half hour after operation these concentrations became somewhat higher—5.9 to 8.3 milligrams per cent and 4 hours after operation they were 6.2 to 8.9 milligrams per hundred cubic centimeters of blood. On the first day after operation, i.e., about 15 hours after insufflation of the culture into the bronchi, the blood levels averaged 8.6 milligrams per cent.

FIGS 1 to 5. Variations in arterial and venous blood gases before, during, and after cyclopropane and oxygen anesthesia.  $\circ$ — $\circ$  represents arterial blood gases,  $\bullet$ — $\bullet$  venous blood gases. The numbers in the abscissae of the graph represent blood studies made at the following time periods: 1, Preoperative and before anesthetic administered; 2, During anesthesia but before incision; 3, during operation and immediately before anesthesia was discontinued; 4, half hour after operation was completed; 5, four hours after operation was completed; 6, first day after operation; 7, second day after operation; 8, third day after operation; 9, fourth day after operation; 10, fifth day after operation. A, represents the blood gas changes presented in the table under part A of the protocol. B, represents the blood gas changes presented in the table under part B of the protocol. C, represents the blood gas changes presented in the table under part C of the protocol.

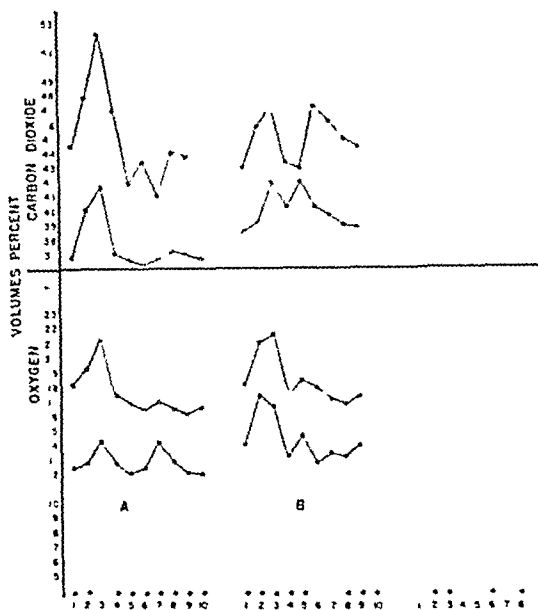


Fig 5 Animal 5

It is noteworthy to mention that in animal 3, in which the sulfapyridine was omitted the night before the gastrotomy was performed, the postoperative blood levels were essentially the same as in the other cases. In all 5 cases there were constant increments in the blood concentrations reaching adequate concentration in the blood within the first 4 hours after operation. The highest concentration attained in this series was 12 milligrams per cent—in animal 4, on the third day after operation.

#### SUMMARY AND CONCLUSIONS

Sulfapyridine may be used prophylactically in the prevention of postoperative pneumonia. When so employed, in the experimental animal, the blood constituent changes and oxygen supply to the tissues are not very different from those seen in the animal making a smooth and uneventful postoperative recovery. In but 1 instance did our animals develop postoperative pneumonia, in which case the course was benign and the animal made complete recovery.

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# GASTROSTOMY IN CASES OF CARCINOMA OF THE ESOPHAGUS

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THERE has been a justifiable dissatisfaction on the part of patients and surgeons alike with the more commonly used methods of performing a gastrostomy. The patient has had to bear the annoyance of wearing a rubber tube and the discomfort resulting from irritation of the skin by the adhesive tape or by the moisture exuding around the catheter. The attendants have had the occasional worry resulting from the accidental escape of the tube and the bother of changing a complicated dressing. The surgeon has been faced with the probability of a high operative mortality and has been anxious to improve on the practicability of the procedure. The recognition of these difficulties led to an interest in this problem and the ensuing report is based upon the study of a group of cases observed at the Massachusetts General Hospital with a few from private practice and the clinic of the Palmer Memorial Hospital.

The purpose of the study was to determine whether anything could be done to improve the comfort of the patient condemned to the use of this artificial method of alimentation or to make easier the details of his care after operation.

Over a period of many years various surgeons have worked upon this problem, attempting usually by some sort of plastic operation on the stomach to construct a fistula which could be utilized for feeding but which would not permit the regurgitation of gastric contents. There is no need to review the details of all of the various unsuccessful methods. Only two methods, the Beck-Jianu and the Spivak, have appeared to be satisfactory in the experience of other surgeons. This study has been carried out with the idea of testing these.

The majority of the patients were seen after all attempts at treatment of the local lesion

by dilatation or irradiation had been carried out. Certain patients were seen, however, while treatment was being given or before it was begun. In the past year the number of patients treated by x-ray without a gastrostomy has increased somewhat and a few have been carried along with varying degrees of success by Dr. E. B. Benedict, who used a modification of the ancient method of bouginage. In a few cases, also, the operation has been advised against because of the moribund state of the patient.

In the study of the cases, for certain reasons, the following data were obtained:

1 *Operative mortality* This had always been thought to be high, largely because of the condition of the patient.

2 *Development of sepsis in the wound* This is important because if a patient is afflicted with a disease which can be expected to end fatally in a few months, any prolongation of the period of immediate postoperative convalescence is to be avoided. Any operation which is apt to be attended by a high incidence of wound infection must therefore be regarded as unsuitable.

3 *Occurrence of leakage from the fistula* Obviously any method which is apt to result in leakage increases the discomfort and adds much to the difficulty of caring for the patient.

4 *Duration of operation* This was recorded merely for the purpose of affording a yardstick for comparison of the various methods as regards the technical difficulty of the operative procedure.

5 *Necessity for using general anesthesia as a supplement to local infiltration* This was also assumed to be a rough measure of the difficulty of the operation. Naturally the more traction and general manipulation necessary, the greater the likelihood of needing a supplementary inhalation anesthesia.



TABLE I—GASTROSTOMIES 1932-1935 IN  
CLASSIFIED BY CATHETER METHODS

	N	%
Total case	2	
Operative deaths	2	100
Wound sepsis	8	39
Leakage	3	14

6 *Experience of the operator* With but few exceptions all of the rubber tube gastrostomies were performed by the interne staff. The majority of the plastic operations were performed by me with a few done by the resident surgeon.

To gain some idea about our experience with gastrostomy for carcinoma of the esophagus before the period of this assignment all the operations performed in the 4 year period 1932 through 1935 were studied. They were all done by one of the various catheter methods (Kader Bann or Witzel) with results as tabulated in Table I. From this it appears that although the operative mortality was lower than anticipated there was too high an incidence of sepsis in the wound and a significant number of cases with leakage around the catheter.

#### PERIOD OF THE SPECIAL STUDY 1936 THROUGH 1939

*Choice of cases* In every case the decision as to the advisability of performing a gastrostomy was based upon its individual merits. At first however because of the presumed greater risk of the plastic operation methods the sickest patients were still operated upon by the simple insertion of a catheter. Only those who were not too old and who were still in a fairly good state of nutrition were chosen for the plastic type of operation. At first the Beck-Jianu method was used. Later with the popularization of the Spivak method the latter was taken up. As experience with these methods was accumulated fewer catheter type gastrostomies were performed and during the past year one or the other of the two plastic types of operation has been used in every case.

*Technique of operation* For the benefit of those who might desire to renew their familiarity with the subject a brief description of each of these operations follows.

1 *Beck-Jianu gastrostomy* This operation was described independently in the year 1902 by Dr. Carl Beck of Chicago and in the year 1912 by a Roumanian surgeon Amza Jianu.

Neither one of these surgeons ever used the operation on a human being. Jianu worked out the technique on human cadavers and suggested it as a method of constructing an artificial esophagus after esophagectomy for carcinoma. In his article describing it a picture showing the gastric tube pulled all the way up on the chest wall to a level opposite the upper extremity of the sternum is given. There are great technical difficulties in the way of carrying out such a procedure in the living patient. It is planned to discuss these details in a future publication. Beck actually proved the value of the operation by performing it on dogs. A German surgeon W. Roepke by name was the first to perform the operation successfully in man.

By the Beck-Jianu method a tube is constructed from the stomach wall along the greater curvature. Figures 1, 2, 3, and 4 will serve to illustrate the steps in this procedure. A left upper quadrant muscle splitting incision is made through the rectus muscle. The right gastroepiploic vessels are ligated and cut at a suitable place near the antral portion of the stomach (Fig. 1). The gastocolic ligament is then divided from that point as far to the left as is deemed necessary to allow the construction of a tube of sufficient length usually about 5 to 6 inches. The left gastroepiploic vessels are retained to carry the blood supply to the gastric tube. Two long curved flexible gastric clamps are then placed on the stomach parallel with the direction of the greater curvature and the stomach (both walls) is cut between them for the desired distance 5 or more inches. The handles of the clamps are separated and the flap is swung out away from the body of the stomach (Fig. 2). The stomach edges are then sutured beginning on the body of the stomach which is closed to form a new greater curvature and extending all the way up the gastric tube to its end. After this the cut edge of the gastocolic ligament is sutured to the stomach wall (Fig. 3). The gastric tube is then brought out of the peritoneal cavity and passed around

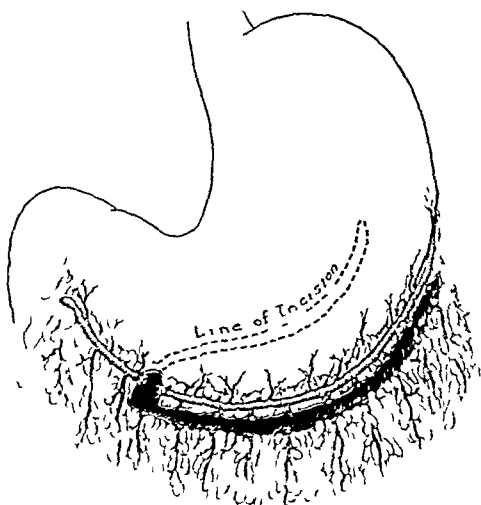


Fig 1 Beck-Jianu gastrostomy Division of the gastrocolic omentum, ligation of the right gastroepiploic vessels Dotted line shows direction and optimal length of incision through stomach walls (Clamps omitted from the drawing)

anterior to the costal margin on the left side, through a subcutaneous channel superficial to the deep fascia, and out through a short transverse incision on the anterior chest wall several inches above the upper end of the abdominal incision (Fig 4)

Important practical technical points in connection with this operation are (a) The incision of the stomach walls *must* be kept parallel with the greater curvature. Otherwise, if it is allowed to deviate proximally toward the lesser curvature, an hour-glass deformity with malfunction because of obstruction will result (b) The newly constructed gastric tube must be drawn tightly around the costal margin and pulled as high as possible on the chest wall. If this is not done, regurgitation will result (c) All the aseptic precautions and refinements of technique which would ordinarily be used in any gastric operation must be observed

2 *The Spivak operation* This was first described by Spivak in 1929. It is an ingenious modification of the Janeway type of operation by which a tube, having at its base a fold of stomach wall which acts as a stop-valve is constructed from the anterior surface of the stomach. The base of the flap may be located

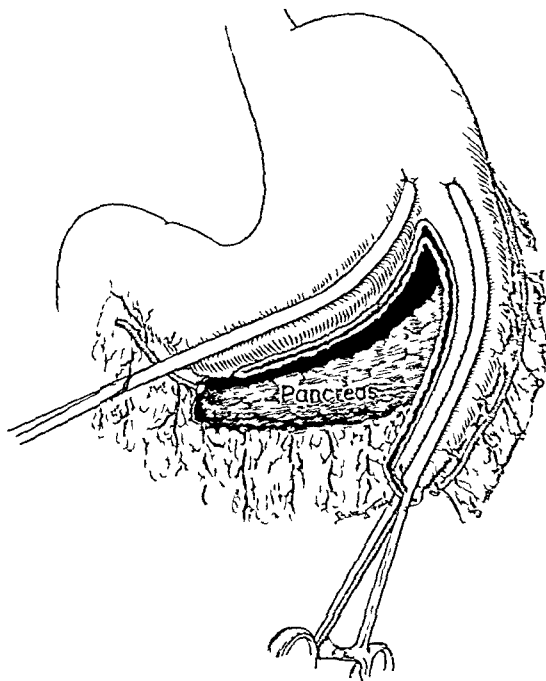


Fig 2 Beck-Jianu gastrostomy Stomach divided and ready for suture Note the preservation of the left gastroepiploic artery on the gastric tube (Clamps shown in place as actually used during the operation)

at almost any point, but is usually placed along the lesser curvature. An instrument such as an Allis forcep is laid on the stomach near the lesser curvature and by sutures the gastric wall is then infolded over the instrument for a distance of several inches (Fig 7). A rectangular flap is then turned back, and the infolded portion is used as its base (Figs 8 and 9). A suture is then begun near the greater curvature and carried transversely across the stomach so as to close the opening and also bring together the two edges of the gastric flap to form a tube (Fig 10). This tube has at its base on the inside of the stomach a fold of gastric wall which stops the opening from within and is supposed thereby to prevent regurgitation (Fig 11). The tube is then brought straight out through the incision and the wound closed around it (Fig 12 and 13).

In the performance of this operation one must (a) avoid injury to the vessels along the lesser curvature, which constitute the only blood supply to the gastric flap. Spivak

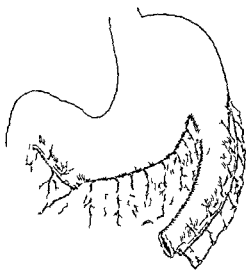


FIG. 3. Beck J. nu gast o tomy. Sutu e of th body f the t mach a d ga t r c tube compl t ed. (a) ocu l l gam nt esutu d to th stoma h. (a) t c t l l s f r dy t be b ught t e the ost l m r g a

stresses the importance of using interrupted sutures for the infolding suture to avoid constricting any of the vessels. (b) Make certain that the tube is long enough by carrying the incision far out onto or even over the greater curvature to the posterior wall. If the stomach appears to be too narrow, the base of the flap can be made crosswise over the anterior surface of the fundus, thus giving the length of the stomach to allow added length to the tube flap.

**Results.** The cases of patients who were treated in the years 1936 through 1939 were studied. Table II presents a summary of the data which were obtained as a result of the experience with gastrostomy at the Massachusetts General Hospital.

During the same 4 year period 8 operations were performed at the Palmer Memorial Hospital, 6 by the Beck-Jannu method and 2 by the Spivak. These have been added to the 26 which were performed at the Massachusetts General Hospital in order to make a larger series for analysis. The results are illustrated by Table III which gives the essential data obtained from the study of these 34 cases in which plastic gastrostomies were performed.

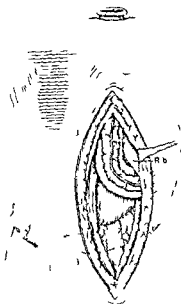


FIG. 4. Beck J. a g t t my. R a t i e p c t f th g t t b after c m p l t i n f th p o t i n. Th tube h s b n b o u h t t a r o i j th costal m r g i p th o u h a s b e t a e u t u n n l n th a n t i r e b e s t w d n d o t t h r o u g h a m a l l t r a n s e c t i o n s v a l i c h e s t e

#### OBSERVATIONS FROM STUDY

It is obvious that the mortality in the cases has remained about the same as in the previous period (193-1936) when the insertion of a rubber tube was the only method used. It is felt that this is dependent upon uncontrollable factors inherent in the nature of the disease and the malnourished debilitated state of the patients. Attention should be called, however, to the fact that the Beck-Jannu and Spivak methods can be done with about as much safety as the simpler catheter methods. One must keep in mind none the less that these so-called plastic gastrostomies are major procedures involving the opening of the stomach and that they require considerable skill in the fundamental technique of

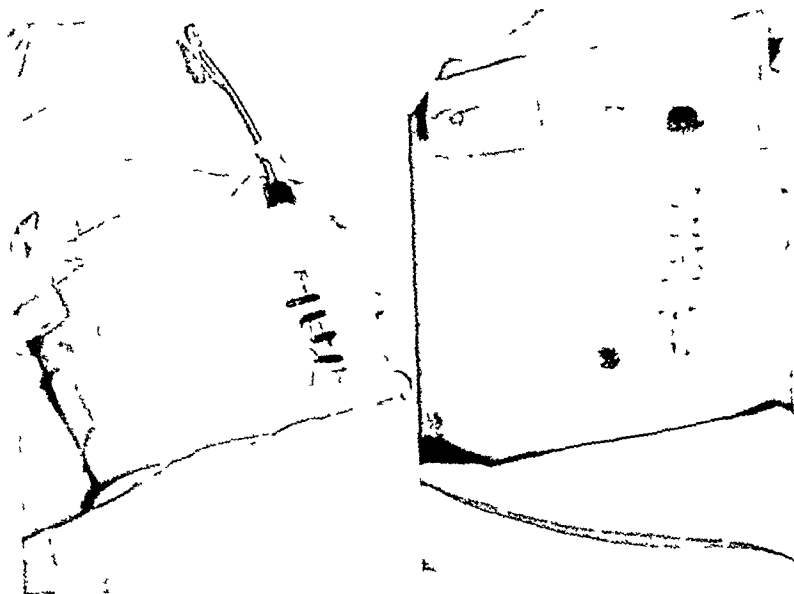


Fig 5, left Beck-Jianu gastrostomy Photograph of patient 1 week after operation, showing temporary catheter in place in the gastrostomy stoma

Fig 6 Beck-Jianu gastrostomy Photograph of a patient 2 weeks after operation

gastrointestinal surgery, such as the careful preservation of the blood supply to the flaps, the accurate placing of sutures, and protection of the wound and peritoneal cavity from gross contamination. They cannot, therefore, be recommended for use by the inexperienced operator. All of the deaths were caused by pneumonia. There was no case of peritonitis.

TABLE II—GASTROSTOMIES FOR CARCINOMA—MASSACHUSETTS GENERAL HOSPITAL SERIES—1936-1940

Method	No	Operative mortality	Sepsis	Leakage	Average duration of operation minutes	Anesthesia supplement
Senn	13	1	1	0	63	2
Kader	7	1	1	0	67	0
Witzel	4	1	1	0	69	1
Total catheter	24	3	3	0		3
Per cent		12.5	12.5			12.5
Janeway	1	0	0	0	60	0
Beck-Jianu	18	2	0	0	64	3
Spivak	7	0	0	1	46	0
Total plastic	26	2	0	1		3
Per cent		7.7				11.5

The average duration of operation is interesting. In general it takes 1 hour to perform a gastrostomy. The catheter methods can usually be done by an experienced surgeon in one-half hour. Of the two plastic methods, the Spivak takes less time than the Beck-Jianu. As has been pointed out, the saving of time is relatively unimportant in itself unless the patient happens to be under general anesthesia. The only fact of importance is that either of the two plastic methods can be done fairly rapidly.

So far as sepsis goes, the tables show that by careful technique it can be almost entirely eliminated. But as one would expect, the

TABLE III—GASTROSTOMIES FOR CARCINOMA—COMBINED MASSACHUSETTS GENERAL AND PALMER MEMORIAL GROUPS

Method	No	Operative mortality		Sepsis	Leakage
		No	Percent		
Beck-Jianu	24	3	12.5	1	1
Spivak	9	1	11.0	0	0
Janeway	1	0		0	0
All plastic methods	34	4	11.7	1	1



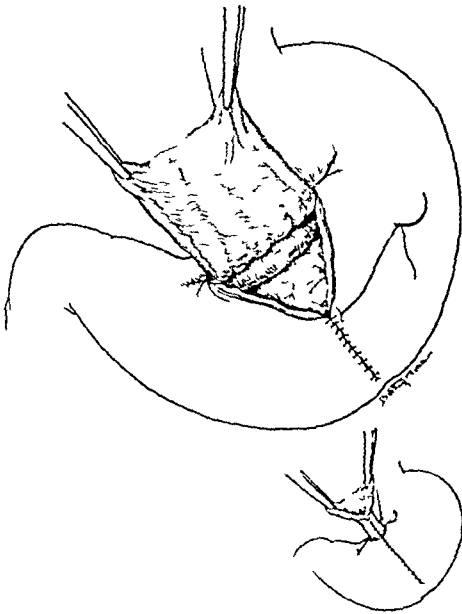


Fig 10 Spivak gastrostomy Closure of stomach begun Insert shows the anterior gastric wall closed and the suture of the gastric tube partly completed

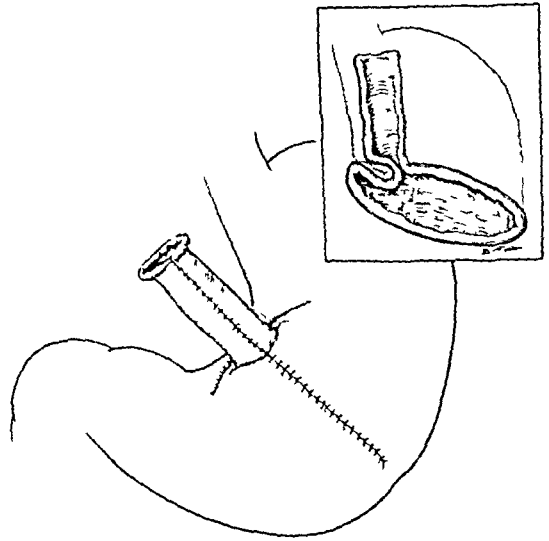


Fig 11 Spivak gastrostomy Closure of stomach wall completed and gastric flap turned in to produce a tube Note a shoulder of stomach wall around the base of the tube, the result of turning in of a fold as the first step Insert shows in cross section the valve-like fold of gastric wall at the base of the gastrostomy tube It is this which prevents regurgitation from within

and feedings can be given by inserting a catheter or the end of a glass syringe with a rubber bulb attached at the appointed times There is no mess and there is much less bother for the attendants The majority of these patients learn to feed themselves just as readily as almost all colostomy patients learn to take their own enemas

The objection is often raised that the stomach is sometimes too much contracted to permit the performance of a Beck-Jianu or a Spivak gastrostomy Experience has shown, however, that after a few minutes of handling at the time of the operation, the stomach will usually relax and stretch out enough to allow one to use either method Rarely there is not

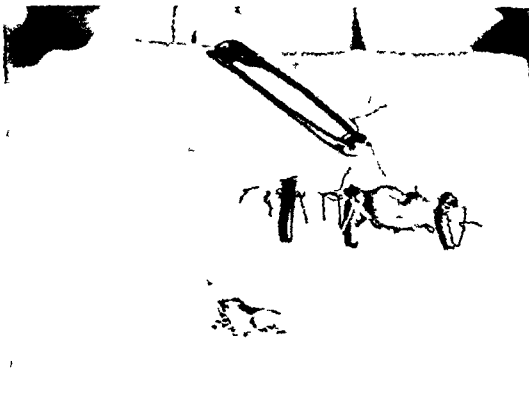


Fig 12 Spivak gastrostomy Appearance of the wound 4 days after operation

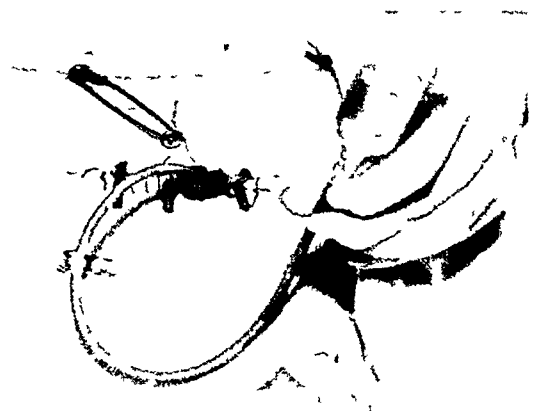


Fig 13 Spivak gastrostomy Injection of fluid by means of catheter and syringe

enough for the safe performance of a Beck-Jianu operation but in all cases the Spivak can be used

#### CONCLUSIONS

1 No gastrostomy should be done on a moribund patient who is suffering from carcinoma of the esophagus. It should be performed as soon as obstruction becomes sufficiently complete to interfere seriously with the patient's nutrition.

2 With care the operative mortality in cases of gastrostomy performed because of malignant obstruction of the esophagus should not exceed 15 per cent.

3 The operative mortality after the Beck-Jianu or Spivak type of gastrostomy should be no greater than that after the catheter methods.

4 The Beck-Jianu or Spivak gastrostomy either one is more comfortable and is easier to care for than are the older catheter types of gastrostomy.

5 The Spivak operation is somewhat easier to perform but regurgitation more likely to occur than after the Beck-Jianu operation.

6 In general the Beck-Jianu operation has been the most satisfactory of all the methods tried.

7 In the last analysis the choice of method of procedure must be made by the individual surgeon on the basis of his experience and technical skill.

8 The interesting suggestion of Beck in 1903 of Jianu in 1912 and of Willy Meyer in 1914 to utilize the Beck-Jianu operation in the reconstruction of an external esophagus after resection in certain favorable cases of carcinoma of the esophagus has been tried in several cases with satisfaction.

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# DISTANT METASTASIS IN CANCER OF THE UPPER RESPIRATORY AND ALIMENTARY TRACTS

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THERE is an abundance of literature dealing with the diagnosis, treatment, and clinical course of cancer of the head and neck, yet relatively little has been written about the terminal pathology in those patients who die from the disease. The incidence of local lymph node involvement is well known and needs no emphasis, yet the frequency with which these tumors produce widespread systemic metastases is often overlooked.

That malignant neoplasms metastasize through lymph vessels, blood vessels, celomic cavities, cerebrospinal spaces, and epithelial cavities is accepted by all students of oncology. Many neoplasms have characteristic but by no means constant, modes of extension through one or more of these paths.

In this paper we shall confine ourselves to the study of distant metastasis from cancer of the upper respiratory and alimentary tracts. In these areas the most common neoplasms are those which arise from squamous epithelium. Their usual path of metastasis is through the lymph vessels to the regional lymph nodes, where the tumor cells are often "filtered out." If the field is fertile, they continue to multiply, producing a concurrent enlargement and destruction of the lymph node. Most squamous carcinomas of the head and neck, if untreated, produce metastases to the cervical lymph nodes. Crile (8), years ago, called attention to the extensive collar of lymphatics about the neck and its effectiveness in preventing the spread of cancer below the clavicle.

Infiltrating tumors frequently invade the walls of veins, penetrate to the lumen, and proliferate intravenously (38). Should fragments of this invading tumor be broken off before the vein is thrombosed, they are carried along in the blood stream and may lodge in the small arteries and arterioles of the lung.

From the Head and Neck Service, Memorial Hospital

Whether metastatic growths develop depends not only upon the proliferative activity of the tumor cells, but also upon the behavior of the tissues in which they are implanted.

That squamous carcinoma has this property of invading veins and producing distant metastases is well known, its frequency, we believe, is often underestimated. Crile (8) quotes Hitchings as finding secondary cancer foci in distant organs and tissues in less than 1 per cent of a series of 4,500 cases of cancer of the head and neck, all of squamous origin. Hitchings' report, however, based on clinical observation, was never published, nor is the source of the material known. From our own experience we have found the clinical determination of visceral metastases far from accurate. Price, in a series of 107 autopsies on patients who died of cancer of the upper respiratory and alimentary tracts, found 14 with distant metastases. He quotes Naegeli, who in 190 cases of primary cancer of the skin and oral mucosa found no metastases in internal organs. Ewing, discussing cancer of the tongue and mouth, states "metastases in the organs are rare, but have been observed in liver, heart, adrenal, and mesentery." McWhorter and Cloud noted a tendency of esophageal cancer to remain localized, due to the fact that ulceration and obstruction terminate the case before distant metastases have time to form. On the other hand, Burke found distant metastases in 27 of 88 autopsies on patients who died from cancer of the upper respiratory and alimentary tracts. Halberstaedter and Simmons are mentioned by Price as having found metastases in 19.3 per cent of the infiltrating types of skin tumors when first seen.

In the records of the Memorial Hospital there are 308 autopsies on patients who died of cancer arising in the upper respiratory and alimentary tracts. Histological examination of the primary tumor was made in 284 cases



TABLE I—THE INCIDENCE OF DISTANT METASTASIS FROM VARIOUS SITES OF ORIGIN

L	f h	ry	number	C mph nod	I m	P rce
			of	ad	ly	d m
Lip			3	0		5
Mucosa of cheek				7		
Floor of mouth			6	2		6
Gum				0	5	36
Tongue			60	3		8.3
Pharynx				5	5	7
Trachea			7	5	5	
Nasal cavity				3		17
Wall of pharynx			8	0		5
Esophagus			38	5		8
Stomach			7			8
Small intestine			36			5
Total			5		66	

Because of the lack of histological proof of the primary lesion the remaining 24 cases are not included in this study. In 278 cases or 91.9 per cent accepted for study the primary growth was squamous carcinoma 6 cases or 2.1 per cent were adenocarcinoma.

Of the 284 cases studied 257 were males and 27 were females a ratio of 10:1. This sex proportion is in keeping with the general admission for this group of tumors. Burke in a similar series found a sex relationship of 92 males to 3 females.

#### DISTANT METASTASES FROM VARIOUS ANATOMIC SITES

The relative frequency of distant metastases from cancer primary in the various anatomic structures is shown in Tables I and II. A more detailed discussion of individual sites of origin follows.

**The lip.** Of the 13 autopsies on patients who died of primary epidermoid carcinoma of the lip 2 had distant metastases 15.4 per cent. Six patients had enlarged clinically metastatic regional lymph node involvement on admission 1 of whom had distant metastases at autopsy. The patient who did not develop distant metastases ranged in age from 41 to 80 years with an average age of 60 years. One patient with visceral metastases was 73

years of age the age of the other was not recorded. There were 12 males and 1 female in the series. Distant metastases were found in the pleura lungs pericardium stomach bones liver and pancreas.

**The mucosa of the cheek.** Four 40 per cent of the 10 patients who died from cancer of the mucosa of the cheek had visceral metastases at autopsy. Regional lymph node involvement was noted in 7 on admission. The average age of patients with distant metastases was 53 years of those with local disease 64 years. There were no females in this group. The lungs and pleura were involved in 17 instances the liver in only 1. In 1 patient squamous carcinoma was found growing in a blood vessel of the lung.

**The floor of the mouth.** There were 16 patients in this series with cancer of the floor of the mouth 7 or 44 per cent of whom had regional lymph node metastases on admission. Only 1 patient aged 74 with regional lymph node involvement showed distant metastases in the lung at autopsy. The microscopic picture in this case was adenocarcinoma—adenoid cystic type. In the other 15 patients the origin of the primary tumor was in squamous epithelium. They ranged in age from 35 to 74 years with an average age of 58. All patients in this group were male.

**The gingiva.** Fourteen male patients had epidermoid carcinoma of the gingiva 5 or 36 per cent of whom showed remote dissemination of the lesion at autopsy. Nine patients had regional lymph node involvement when first seen. The ages of the entire group ranged from 45 to 78 years with an average age of 61 and 63 respectively for those with and without distant metastases. These patients showed the widest distribution of metastatic lesions of all groups studied. The lungs were involved 4 times the pleura myocardium and adrenal twice while the diaphragm pericardium stomach spleen mesenteric lymph nodes and skeletal system were each involved once.

**The tongue.** Of the 60 patients who died of cancer of the tongue 30 had lymph node involvement on admission and 11 or 18.3 per cent showed distant metastases. The distant metastases were widely distributed the

TABLE II—THE DISTRIBUTION OF DISTANT METASTASES IN 284 AUTOPSIES

Location of primary growth	No of autopsies	Distant metastases	Lungs	Liver	Pleura	Pericardium	Heart	Bone	Diaphragm	Peritoneum	Stomach	Spleen	Adrenals	Kidney	Intestine	Brain	Pancreas	Bladder	Skin	Skeletal muscles
Lip	15		1	1	1	1		1			1						1			
Mucosa of cheek	10	4	2	1	2															
Floor of mouth	16	1	1																	
Gingiva	14	5	4		2	1	2	1	1		1	1	2							
Tongue	60	11	5	5	1	2	2	2	2											
Palate	11	3	1	1	2		1	1	1	1						1		1	1	1
Tonsil	27	3	1		1					1										
Nasal cavity and sinuses	14	5	3	3	2	1						1		1						
Wall of pharynx	8	2	2	1	1						1									
Extrinsic larynx	18	7	5	3	1	1					1									
Intrinsic larynx	17	2	1	1																
Esophagus	56	21	6	8	2				1	3		2		1	2	1				
Total	284	66	57	34	18	6	5	5	5	6	4	4	2	2	2	2	1	1	1	1

lung being involved 8 times, the liver 5, the pleura 4, the myocardium, pericardium, diaphragm and skeletal system twice each. In 1 patient squamous carcinoma was found growing in the pulmonary blood vessels. The average age for patients with distant metastases was 52 years as compared with 59 years for those in whom the lesion remained localized. There were 55 males and 5 females in this group.

*The palate.* There were 11 patients in whom the primary lesion was found on the hard and soft palates, and 3, or 27 per cent, showed distant metastases at autopsy. The microscopic picture showed epidermoid carcinoma in 8 cases and adenocarcinoma in 3—salivary gland origin. Five patients had regional lymph node involvement on admission. The 3 patients with adenocarcinoma at no time had regional node involvement, although they lived for 1, 6, and 17 years, respectively, from onset of disease, and 2 showed visceral metastases at autopsy. Extensive dissemination of the tumor was found in 1 of the 8 patients with squamous carcinoma. In the 3 cases with distant metastases the pleura was involved in 2 instances while the liver, peritoneum, bladder, adrenals, myocardium, skeletal system, skeletal muscles, lungs, skin,

and choroid plexus were each involved once. The average ages of patients with metastases and of those whose lesions remained localized were 60 and 64 years, respectively. There were 9 males and 2 females in the group.

*The tonsils and fauces.* Autopsies were performed on 27 patients who died of epidermoid carcinoma of the tonsil, 3, or 11 per cent, of whom showed distant metastases at autopsy. Eighteen had regional lymph node involvement on admission. The pleura, lungs, and peritoneum were each involved once. All 3 cases showed cancer cells in the mediastinal lymph nodes. It is impossible to state whether these nodes were secondarily invaded from the visceral metastases, by lymphatic extension from the primary tumor, or from the metastatic disease in the cervical lymph nodes. There were 25 males and 2 females in this series. The youngest patient was 40, the oldest 75, with average ages of 61 and 59, respectively, in those with and without distant metastasis.

*Nasal cavity and paranasal sinuses.* Of the 14 patients with cancer of the nasal cavity and paranasal sinuses, the lesion remained localized in 9, while 5 (35.7 per cent) showed distant metastases. Three patients had regional lymph node involvement when first



Fig. 1. Larynx specimen showing the soft plate, meta-tas, n. myoca dum, C. sub p. ca. dial m. ta. t. s. Add. t. n. l. met. tas. w. re. f. und. n. skin. se. sa. l. r. d. n. l. bladder muscles chor. l. p. l. x. th. ra. c. ert. bra. nd. r. b. s.

seen. There were 13 epidermoid carcinomas and 1 adenocarcinoma in this group. Distant metastases all of epidermoid morphology were found 3 times in the lungs and liver twice in the pleura and once each in the pericardium, spleen and kidneys. The average age of the 5 patients with distant metastases was 55 years with localized disease. 57 years. This series had the most even sex distribution there being 8 males and 6 females. Two women and 3 men had visceral metastases.

**The pharyngeal wall.** Autopsies were performed on 7 males and 1 female with epidermoid carcinoma of the pharyngeal wall of whom had distant metastases at death. They were the youngest in the series aged 6 and 40 years respectively and the microscopic picture in both instances was small spindle cell epidermoid carcinoma grade III. Six patients had regional lymph node involvement on admission. Distant metastases were found in the lungs in 2 instances while the pleura

stomach perigastric nodes and liver were each involved once.

**The extrinsic larynx.** A study of the autopsies of 38 patients who died from cancer of the extrinsic larynx showed 7 with visceral metastases (18.4 per cent) 6 of whom had cervical lymph node involvement on admission. Among those in whom the lesion remained localized in the neck there were 19 with metastases in the cervical lymph nodes when first examined. Distant metastases were found in the lungs 5 times in the liver 3 times and in the pleura pericardium and stomach once each. The youngest patient in this group was 38 years old the oldest 78. The average age of patients with distant metastase was 58 as compared with an age of 60 years for those with local disease only. There were 37 males and 1 female in this group.

**The intrinsic larynx.** In the 17 male patients with primary cancer of the intrinsic larynx distant metastases were found in the lungs and liver in 1 patient aged 76 and in the mediastinal nodes in another aged 61—11.8 per cent. Only 1 patient had regional lymph node metastases on admission. The low incidence of both cervical lymphatic and visceral metastases emphasizes the tendency of cancer in this location to remain localized for many months. The youngest patient was 46 years of age the oldest 91. The average age of all patients without visceral metastasis was 62 years.

**The esophagus.** Autopsies were performed on 56 patients who died from cancer of the esophagus 21 or 37.5 per cent of whom had distant metastases at death. The primary lesion was located in the upper third in 11 cases 20 per cent in the middle third in 6 cases 46 per cent and in the lower third in 19 cases 34 per cent. There were cervical lymph node metastases in 2 cases when first seen. In 1 case the primary tumor was in the upper third in the other in the middle third.

As one might expect there was a definite increase in metastases to the thoracic and abdominal viscera in the lower lesions. Of the 11 patients with tumors arising in the upper third of the esophagus visceral metastases were found in only 1 or 9 per cent in

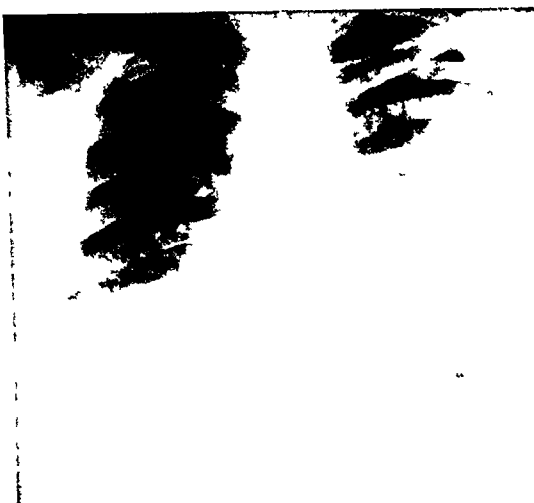


Fig 2 X-ray film of chest showing pulmonary metastases from squamous carcinoma of the tongue. Note the elevation and fixation of the left diaphragm and the shifting of the mediastinal contents to the right. The infiltration in the lower lobe of the left lung might easily be confused with an inflammatory process. At autopsy multiple metastases were found in the left pleura and the heart, while the lower lobe of the left lung was completely infiltrated with the tumor.

the middle third in 9 of 26 cases, or 34.6 per cent, while in the lower third dissemination was present in 11, or 58 per cent, of the 19 cases. In the 21 patients with visceral metastases the liver was involved 8 times, the lung 6, the peritoneum 3, the pleura, spleen, and intestines twice each, the diaphragm, kidney and brain once each. The mediastinal lymph nodes were invaded by cancer cells in 10 instances.

There was no appreciable age difference for the 3 levels. The youngest patient was 25 years of age, the oldest 80. The average age for patients with visceral metastases was 55 years, without visceral metastases, 59 years.

THE INCIDENCE OF METASTASIS  
IN DIFFERENT ORGANS

The tendency for many tumors to produce metastasis in certain special organs or structures is well known. Rarely, we believe, is metastasis the result of the migration of a single cancer cell or of a single shower of cancer emboli, nor can it be explained in terms of vascular distribution. Cancer cells must frequently be carried to the skeletal muscles,



Fig 3 Metastatic squamous carcinoma in a thrombosed blood vessel in the lung. The primary tumor was in the mucosa of the cheek. This is evidence of the thrombotic origin of some metastases. Additional metastases were found in perivascular lymphatics and in alveoli—all probably secondary to hematogenous metastases. A, blood vessel wall, B, cancer cells, C, cancer cells in perivascular lymphatics.

yet rarely are these tissues involved. It becomes apparent that some tissues provide the optimal chemical or metabolic qualities necessary for the growth of special tumors. Willis, Boyd, and others have emphasized this point. The distribution of distant metastases is shown in Table II.

*Lungs* (Figs 2, 3, 4). Although in head and neck cancer it is possible for the lungs to be-



Fig 4 Longitudinal section through lungs showing diffuse permeation of the pulmonary lymphatics metastatic from squamous carcinoma of the tongue.



Fig 5 Metastatic lung nodules from carcinoma of the stomach. The metastatic nodules are seen in the lung tissue, some of which are surrounded by a lymphatic reaction.

come invaded by secondary cancer growths either by direct extension from the primary tumor or by way of the lymphatics almost all metastatic neoplasms in the lungs arise from blood borne tumor emboli which have lodged in arteries or arterioles. In our series tumor cells were found growing in both pulmonary arteries and veins. When secondary neoplastic disease has become established in the lungs invasion of the pulmonary veins can readily produce wide systemic dissemination of tumor emboli. In our 228 cases of oral nasal and pharyngeal cancer metastases were found in the lungs in 9 or 12.7 per cent and in 6 or 10.7 per cent of 56 cases of esophageal cancer.

*Liver.* Tumor emboli entering the liver may arrive by way of the lymphatics the portal vein or the hepatic artery. Metastases from primary tumors of the head and neck reach the liver by the latter route. Should other abdominal viscera or retroperitoneal lymph nodes be involved it is conceivable that these secondary growths might in turn produce liver metastases through the portal vein or regional lymphatics. Willis found the liver to be involved in 116 or 36 per cent of 323 autopsies. He quotes Colwell as finding the liver involved in 24 per cent. Kettle 25 per

cent and Kaufman 26.5 per cent of all patients who died from cancer. These authors gave no figure for head and neck tumors. In a group similar to ours Burke found metastases in 8 of 54 autopsies. We noted liver metastases in 16 or 7 per cent of the oral and pharyngeal groups and in 8 or 14 per cent of the esophageal tumors.

*Pleura* (Fig 5). Eighteen or 6.3 per cent of our autopsies revealed metastatic cancer on the pleura the primary tumor being located in the esophagus in 2 patients. In 3 instances extensive invasion of the diaphragm was associated with pleural metastases. It is of interest to note that pleural metastases without lung invasion were found in only 4 cases. In 2 patients diffuse bands of carcinoma were seen growing in the pulmonary lymphatics from the pleura to the hilum of the lung.

*Heart and pericardium* (Fig 1). Tumor invasion of the heart and pericardium by continuity of tissue from lung bronchus esophagus and mediastinal lymph nodes has been observed many times. Venous invasion by continuity of growth along the superior and inferior vena cavae is well known. Tumors of the thyroid and kidney are especially prone to extend in this manner. They seldom invade the myocardium however but remain as intracardiac growths. Secondary cancer foci in the myocardium are the result of tumor emboli occluding coronary arteries or arterioles and are usually associated with widespread blood borne metastases. A review of the literature including all groups of cancer gives the incidence of metastases in these sites as 0.28 per cent to 6.2 per cent in fatal cases. Willis found 20 cases with myocardial metastases the primary tumor was located in the tongue in 2 instances and in the lip and pharynx once each. Burke found 3 patients with myocardial metastases from cancer of the upper respiratory and alimentary tracts. In our series the pericardium was involved 6 times—2.1 per cent—the myocardium 5 or 1.76 per cent.

*Skeletal system.* The literature dealing with the incidence and mechanism of blood borne metastases to bone is extensive. The frequency of skeletal metastasis is exceeded only

by that in the lungs and liver, and if all groups of tumors are included, the percentages vary from 15 to 30 per cent. A much higher figure is obtained in those groups which seem to have a special affinity for bone, such as breast, prostate, thyroid, and kidney. On the other hand, it has been pointed out by Willis, who cited Rolleston, Derigs, Joll, and Gardham, that epidermoid carcinoma of the mouth and pharynx rarely yields skeletal metastasis. He found that cancer of the esophagus produced metastases in bone in 15 of 273 cases collected from the literature. Multiple skeletal metastases with wide systemic dissemination were noted in 5 of our cases—1.76 per cent.

*Other organs.* Distant metastases to other tissues were less frequent. From the literature we were able to collect 17 cases of metastases to the kidney from cancer of the upper respiratory and alimentary tracts, to which we add 2 of our own. Blood-borne metastases to the stomach and intestines are rare, as we found only 6 cases in our series—4 in the stomach and 2 in the intestine. From the literature we collected 144 cases of intestinal metastases, and in only 1 instance was the primary lesion found in the areas studied in this paper. It was a case of cancer of the pharynx. In these groups of tumors, metastases to other tissues, such as brain, skeletal muscles, spleen, pancreas, and bladder, appear to be extremely rare. We could find no instance in the literature reviewed in which these tumors metastasized to the generative organs of either sex.

#### FACTORS INFLUENCING DISTANT METASTASIS

*Syphilis.* Many eminent authorities believe syphilis to be a causative factor in the production of intraoral cancer. Its importance, if any, in the development of visceral metastases is rarely mentioned. Burke noted distant metastases in 4 of 20 patients with positive Wassermann reactions out of 186 cases of squamous carcinoma. In our series, complement fixation was positive for syphilis in 19 of 94 patients tested. Syphilis, however, was of no etiological significance in the production of distant metastases, as in only 3 instances were the 2 conditions associated.

*Age.* In this series of autopsies we found little evidence to substantiate the common

TABLE III—RELATIONSHIP OF DURATION OF DISEASE TO DISTANT METASTASES

Location of primary growth	With local disease only at autopsy		With distant metastases at autopsy	
	Onset to admission—mo.	Onset to death—mo.	Onset to admission—mo.	Onset to death—mo.
Lip	10	48	5	9
Mucosa of cheek	6	11	10	21
Floor of mouth	5½	32	4	5
Gum	16	20	6	9
Tongue	8	15	9	15
Palate	6	6	32	92
Tonsil	6	17	4	10
Nasal cavity and sinuses	22	15	6	10
Wall of pharynx	13	27½	2½	7½
Intrinsic larynx	6½	12½	4½	10
Esophagus	4½	7	6	8
Average	9.6	19.6	7.6	14.4

contention that cancer in the aged tends to run a comparatively benign course while cancer in the young tends to be exceptionally malignant. The statement may be true within certain limits, but the decreased resistance of the aged to the associated local infection and their susceptibility to pulmonary diseases largely offsets any advantage afforded by lesser tumor activity. Occasionally, even in the presence of old age, metastases were widely disseminated throughout the body. The average age of all patients who had cervical lymph node metastases on admission and later were subjected to autopsy was 58 years as compared with 59.5 years for those in whom the local lesion was the only evidence of disease. However, the 66 patients with visceral metastases had an average age of 55.8 years as compared with 59.4 years for patients without distant metastases.

*Duration of disease.* We reviewed our cases with the thought in mind that patients with epidermoid carcinoma who gave a longer history of disease before treatment might have a relatively higher incidence of visceral metastases, but such was the case in only the cheek mucosa and esophageal groups. In the other groups a shorter history, both from onset to treatment and onset to death, was found in

patients with distant metastases. In the very small group of adenocarcinomas (6 cases) however the longest durations of disease (6 and 17 years respectively) were found in 2 palatal cases which showed metastases in the lungs and pleura at autopsy (Table III).

**Cervical lymph node metastasis.** Since the most common site for metastases from epidermoid carcinoma is the regional lymph nodes and since the more anaplastic the tumor the greater the frequency of node involvement we attempted to determine whether cervical lymph node metastasis had any connection with the incidence of visceral metastasis. In Table I we show the incidence of cervical lymph node metastases on admission and visceral metastases at autopsy. Although the tumors of the pharyngeal group i.e. tonsil pharyngeal wall and extrinsic larynx had a high incidence of cervical metastases relatively few showed involvement of distant organs at death. Of the 117 patients with oral nasal pharyngeal and laryngeal tumors associated with metastatic lymph node disease on admission 31 or 25.5 per cent had visceral metastases while 14 or 10.3 per cent of 111 patients with local disease only when first seen showed metastases in distant tissues at autopsy. It is noteworthy that in our series no patient with epidermoid carcinoma had visceral metastases who did not have cervical lymph node involvement at some time during the clinical course of his disease. Two patients with adenocarcinoma of the palate had visceral dissemination of the lesion without ever having had cervical metastases.

**Morphology.** The tumors were graded histologically in 254 patients (Table IV). We have added a group designated as grade II plus in which the tumors were more anaplastic than the usual grade II. The pharyngeal groups showed a higher percentage of grade III tumors yet the incidence of visceral metastases in these was less than in the mucosa of the cheek gingiva and tongue group where the histological picture was predominantly grade II. Taken as a whole a slightly higher proportion of distant metastases was noted in grade III tumors than in any other yet excepting grade I it would seem that the anaplasia of the tumor is of little prognostic value in estimating the probability of visceral metastases.

#### SUMMARY

1 The incidence of distant metastases from cancer of the upper respiratory and alimentary tract has been determined in 284 patients who died from cancer in these areas. Sixty three patients or 23.3 per cent were found to have blood borne dissemination. The most common sites for distant metastases are lungs liver and pleura in the order named.

2 Patients who died from cancer of the mucosa of the cheek gingiva palate nasal cavity and esophagus showed the greatest percentage incidence of systemic dissemination of the primary lesion.

3 Patients with distant metastases gave a shorter history from onset of disease to treatment and from onset to death than patients in whom the tumor remained localized.

4 It was impossible to determine the probability of visceral metastasis from the morphology of the tumor or the age of the patient. However the average age of patients with distant metastases was less than that of patients in whom there was only local disease.

5 The incidence of distant metastases at autopsy in patients with cervical lymph node involvement on admission was two and one half times that of patients in whom the local lesion was the only evidence of disease at the first examination. No patient with epidermoid carcinoma of the mouth nasal cavity

TABLE IV—NUMBER OF PATIENTS WITH (1) LOCAL DISEASE ONLY AND (2) DISTANT METASTASES IN EACH HISTOLOGICAL GRADE OF EPIDERMOID CARCINOMA

	Local disease only	Distant metastases	Total
Grade I			
Grade II			5
Grade II plus		6	3
Grade III			5
Grade IV			
Grade undetermined	1	2	3

pharynx, or larynx had blood-borne metastases in distant tissues who did not, at some time during the clinical course of his disease, have cervical lymph node involvement

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# BACTERIAL CONTAMINATION OF WOUNDS FROM THE AIR FROM THE SKIN OF THE OPERATOR AND FROM THE SKIN OF THE PATIENT

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IT is generally recognized that infection occurs in approximately 3 to 5 per cent of clean surgical wounds (3 4 5 6 7 8 11 12 14 15 4 5 27 8 29 37 39 40 41 42). The majority of these infections must result from a break in the aseptic technique or from some fault inherent in the technique. Methods are available for the absolute sterilization of gowns drapes dressings instruments sutures gloves and solutions. Only through some gross error can these materials become a source of contamination. If one considers operating room procedure in its entirety however it is apparent that three sources of bacteria which are not readily controllable are involved in every operation. These are (1) the air (2) the hands and arms of the surgeon and his assistants (3) the patient's own skin.

In this paper the importance of these sources of contamination is discussed and the methods which have been proposed for their control are evaluated.

## AIR

The fact that bacteria are always present in the air of occupied operating rooms and that they fall on the sterile field has been demonstrated repeatedly (18 23 25 29 31). It is also well recognized that the number of bacteria in the air can be reduced by rapidly changing the air (16 38) by irradiating it with ultraviolet light (17) by the use of germicidal aerosols (36) or by a combination of these methods (38). Hart (16 21) has shown and it has been confirmed in our own operating rooms that the air of an unoccupied operating room provided it is supplied with washed air is nearly sterile. Furthermore if the floor is mopped after each operation very

few organisms can be recovered from such a room even though the air be agitated with electric fans. The bacterial count of the air rises however as soon as members of the operating team enter which suggests that the bacteria are derived from the occupants of the room.

The facts enumerated are well known and accepted but there are two questions regarding the bacterial flora of the air which are still unanswered.

A. What is the source of the bacteria of the air of operating rooms?

B. Are these bacteria from the air responsible for the majority of wound infections?

A. *The source of the bacterial flora of operating room air.* Some observers hold that nearly all of these organisms are derived from the respiratory tract of members of the operating team (21). There is no doubt that the nose and throat of members of the operating team contribute bacteria to the air. Hirshfeld and Laube have shown that surgical masks are only partially effective and that especially during talking a significant number of organisms escape either through or around a mask. They also demonstrated however that very few bacteria are expelled from the nose or throat during quiet breathing and that the maintenance of silence keeps the organisms from the source at a low level. The respiratory tract therefore may be regarded as the source of at least a portion of the organisms. The exact number contributed in this manner depends chiefly upon the amount of talking done by the operating team and the type of mask worn.

What are the other possible sources? Crumkshank recovered hemolytic streptococci from the air of wards housing badly burned patients who were already infected with this organism. White found hemolytic strepto-

cocci in the dust of rooms occupied by patients with puerperal sepsis caused by organisms identical serologically with those recovered from the dust. The streptococci found in the air by Cruickshank were presumably derived from the dried exudate on the dressings of the burned patients and those recovered by White came from the dried lochia of the patients with puerperal sepsis. The findings of these workers show that bacteria which escape from sick individuals in such discharges as those of draining wounds, intestinal fistulas, the parturient uterus, and infected burns, contaminated clothing, bedding, and dressings from which slight agitation sends them flying into the air on small particles of lint, dead epithelium or dried pus. Once in the air they may contaminate the clothing of other individuals and be carried about the hospital.

Staphylococci predominate in all bacterial analyses of operating room air but they do not predominate in cultures of the nose and throat. There is, however, an unlimited source of staphylococci on the skin and hair of the body. This suggests that normal individuals may shed staphylococci on dead epithelial cells, particles of dandruff, and pieces of hair. The following facts strengthen this belief.

a If the eyebrows or hair are gently agitated over an open Petri plate of blood agar from 20 to 100 colonies of staphylococci will be found upon the plate after incubation.

b Similar results may be obtained by gently scraping the skin of the arm or by shaking the hem of a nurse's uniform or an orderly's coat.

c An astounding number of organisms, the majority of which are staphylococci, may be recovered both upon Petri plates and in the Wells air centrifuge from the air of a room in which a bed is being made.

Since bacteria are contributed to the operating room air by dandruff, epithelial cells, hair, dust, and lint from the clothing of the operating team and the patient, experiments were designed to determine the importance of these sources. An operating room supplied with washed air in sufficient quantity to provide  $3\frac{1}{2}$  changes an hour was selected. The room was sealed to prevent leakage about the door and windows. Petri plates were placed in

various locations about the room, some being exposed on the supply tables and on the instrument stand. These were usually exposed for 15 minute periods. The Wells air centrifuge was used to take 10 cubic feet samples of air at the beginning of each 15 minute period. Sampling both by the Petri dish method and the Wells air centrifuge was generally started one hour before any one entered the room and was continued while the nurses set up the room, and the operation was carried out. Members of the team entered the room by the door through which air was discharged to avoid bringing bacteria in from the corridor. Once an individual had entered he remained until the experiment was terminated and only those people necessary for the conduct of the operation were allowed in the room. The results of this investigation may be summarized as follows.

a There is a slight rise in the bacterial content of the air when two nurses enter to set up the room.

b There is a marked rise in the bacterial content of the air, in fact it reaches its highest peak, while the patient is being anesthetized, postured on the table, draped, and the surgeons are donning their gowns.

c As soon as the operation has started and active movement in the room is at a minimum, the bacterial content of the air sinks to a fairly low level where it remains until the operation has ended and there is again considerable movement in the room. At this time the bacterial count again rises abruptly.

d The bacterial counts as recorded by both the Petri plates and the Wells air centrifuge run roughly parallel suggesting that the bacteria are carried on dust particles and that droplet nuclei do not predominate.

e The average bacterial content of the air as well as the marked peaks which occur at the time of draping the patient and again at the end of the operation can be greatly reduced by measures designed to control dust, dandruff, lint, etc. These are donning of sterile clothes by members of the operating team immediately before entering the room, draping the patient except for the operative area with sterile drapes before his entrance into the room, avoiding rapid movements, and also

coating the floor with glycerine. The bacterial content of the air is not greatly influenced by observing silence. This is probably because ordinarily little talking is done in the operating room and the maintenance of silence does not result in a large enough decrease in the number of organisms expelled from the nose and throat to manifest itself in the bacterial content of a room of 5 000 cubic feet capacity. Talking however discharges bacteria directly over the wound and although the total count in the room may not increase significantly the number of bacteria falling into the wound may be greatly increased. For this reason all members of the operating team should maintain silence.

The facts lead one to the conclusion that there are two main sources supplying bacteria to the air of operating rooms:

a. The respiratory passages of the occupants which supply a fairly constant number of organisms all the while the exact number varying with the amount of conversation and the type of mask.

b. Dust, dandruff, lint and dead epithelial cells from the hair, clothing and skin of the operating team and from the clothing and bedding of the patient which cause the peaks that occur during the periods of commotion.

It is possible that some of the bacteria from sources in paragraph b are originally derived from the nose or throat and are merely secondarily transported on the skin and clothing. Be that as it may, the fact remains that the sources listed in paragraph b contribute a significant number of bacteria to the operating room air.

*B. Are these bacteria from the air responsible for the majority of wound infections? That these bacteria are responsible for the majority of wound infections has not yet been proved. In order to prove that bacteria from the air are or are not responsible for the majority of wound infections one must be able to eliminate them by operating in a sterile atmosphere. To date this has not been accomplished although Gudin has achieved this end in part by a complicated system of air sterilization and operating room technique and Hart (19) has greatly reduced the number of bacteria in the air of his operating room by irradiating the*

air with ultraviolet light. The fact that Gudin claims to have reduced the incidence of infection by his method tend to show that bacteria from the air are of some importance. Figures on the incidence of infection in wound made in an irradiated atmosphere have been published by Hart (19, 20) and by Overholt and Betts. They report that ultraviolet irradiation reduced the incidence of wound infections and they attribute the reduction to the decrease in the aerial flora. This is entirely possible but before accepting this explanation one must consider two others.

a. Bacteria may enter a wound from sources other than the air and the ultraviolet light may kill these organisms after they have reached the wound.

b. The ultraviolet light has a definite effect upon the tissues of a wound which may render them more resistant to infection.

In so far as we know there is no evidence to prove or disprove the statement that ultraviolet light will kill bacteria in a wound. It is conceivable however that radiation of the adjacent skin decreases contamination from this source and that radiation of the wound kill many bacteria which escape into the wound through holes in the operators' gloves (10).

Krais et al. have demonstrated that ultraviolet light of 150 Angstroms has a definite effect upon tissues and they quote various workers who believe that irradiation has a beneficial effect upon the wound itself. There is also some evidence that certain amounts of x-radiation increase the resistance of the peritoneum to subsequent bacterial invasion (11). Radiation of a wound may render it more resistant to infection.

It is important to determine which of these explanations of the decreased incidence of infection observed by Hart in wounds made in an irradiated atmosphere is correct. If the elimination of aerial bacteria is the end to be achieved it becomes necessary to irradiate the entire room. If the changes in the wound produced by radiation are the cause of the lower incidence of infection it will only be necessary to radiate the wound. Only when these problems have been solved can ultraviolet radiation be used intelligently.

## THE SKIN OF THE OPERATOR

Surgeons have been offered a great variety of methods for the preparation of their hands, but until Price published his papers (23, 24) on the bacterial flora of the skin they were at a loss to determine the effectiveness of any of these methods. Price is the first worker to present a simple and reliable method by means of which the bacteria on the skin may be counted, and the effect upon them of scrubbing or the application of germicides can be studied. Two facts have come out of his work which are especially pertinent to this discussion.

a. Complete sterilization of the skin of the hands and forearms is so difficult that practical considerations render it an impossibility.

b. The bacterial flora which remains on the skin after scrubbing doubles itself every 30 minutes beneath dry gloves and every 50 minutes beneath wet gloves.

In order to convince himself of the truth of the latter rather startling statement the author cultured gloves which had been worn for varying periods. The number of organisms recovered varied from 1,000 to over 1,000,000 depending upon the individual, the amount of perspiration in the glove and the length of time it had been worn. This demonstrates that an enormous number of bacteria may escape from a torn glove in a drop of sweat. The hazard presented by a torn glove is greater than that offered by the air since ordinarily only 50 or 60 bacteria per hour fall into a wound from the air.

Devenish and Miles have traced an epidemic of *Staphylococcus aureus* wound infections to this source. They found that of two surgeons who were doing most of the operating in their hospital, only one was cursed with wound infections. Both of these men were nasal carriers of a virulent strain of hemolytic *Staphylococcus aureus*, but the one whose wounds became infected also carried a virulent strain of hemolytic *Staphylococcus aureus* on his hands. Tests showed that these organisms passed through the sleeves of his gown which was made of coarse linen (48 threads to the inch). They also passed through holes in his gloves. Punctured gloves proved to be very common, the incidence of holes in 6,585 patched and unpatched gloves being 24

per cent and in 380 unpatched gloves 14.5 per cent. When precautions were taken to prevent this source of contamination by wearing over-sleeves of batiste<sup>1</sup> and taking care to avoid puncturing gloves, the infections ceased.

A check of the gloves in our own operating rooms revealed a puncture incidence of 18 per cent in 120 gloves. In most cases the members of the operating team did not realize that their gloves had been torn.

While the work of Devenish and Miles needs confirmation by other workers, it seems to be very important. It raises immediately the possibility that some of the wound infections previously thought to be due to droplet spray from the nose and throat may have come about because the surgeon harbored on his hands the same organism that he carried in his throat. Price (24) has shown that when the skin is constantly exposed to certain bacteria they may become part of its resident flora. Gillespie et al. found that of 150 medical students 33.4 per cent were nasal carriers of virulent strains of staphylococci while 10.5 per cent were skin carriers and 12.6 per cent were double carriers. The recovery of bacteria which are serologically identical from an infected wound and from the nose or throat of a member of the operating team does not entitle one to assume that the infection occurred via the air. It is necessary first to ascertain that the individual in question does not carry the same organism on his hands and that he did not puncture his glove. Just how many infections occur through the air and how many as the result of torn gloves remains to be demonstrated. It punctured gloves prove to be the chief cause of infected wounds, radiation of the air may not be necessary, and the present practice of wearing extremely thin gloves will have to be changed. The gloves worn by most surgeons at present are so delicate that they are torn with great frequency. It is interesting to recall that Harvey Cushing, who had an extremely low incidence of infection in spite of his lengthy operations, always wore heavy gloves.

## THE SKIN OF THE PATIENT

It is difficult, if not impossible, to evaluate the role played by the patients' own skin in

<sup>1</sup>Brit. Pharm. Codex 1934, p. 1136.

the production of infected wounds. In some clinics great care is taken to cover the skin with sterile pads while in others no attempt is made to protect the skin adjacent to the wound. Occasionally surgeons employ nothing more in the way of skin preparation than simple removal of the grease and dirt with benzene (30) while others paint it with powerful germicides (2). In spite of these differences in technique the reported incidence of wound infection in different clinics does not vary markedly.

These observations would seem to indicate that the skin of the patient is not as important as some other sources of contamination. The explanation probably lies in the facts which Price has made available (33, 34, 35). He has shown (33, 34) that there are two bacterial flora on the skin: the transient and the resident. The transient flora is loosely attached to the skin and is composed of bacteria which have been picked up by the individual from his environment and it varies from day to day in quality and quantity. It is scant on clean protected skin and profuse on dirty greasy exposed areas of the body. The bacteria composing the transient flora are easily removed by a few minutes of scrubbing. The resident flora on the other hand is for a given individual quite constant. The bacteria composing it are so tightly attached to the skin that theoretically  $2\frac{1}{2}$  hours of continuous scrubbing with soap and water are required to remove all of them (34). It is not likely that many of the resident flora are brushed into the wound by the touch of an instrument or gloved hand. In addition the germicides which are commonly applied to a clean skin certainly destroy or at least inhibit the growth of many loosely attached bacteria. It is those organisms which are tightly attached to the skin which survive the application of germicides. Some chemical germicides notably the mercurials do not destroy the organisms but imprison them beneath a tough impervious film (35) which protects the wound.

It is the author's opinion that the importance of the resident flora on the patient's skin as a source of wound infection has been exaggerated. If the skin is properly freed of

transient bacteria the tightly resident flora probably do not present a serious hazard. However, no one has been able to prove this contention one way or another and until some one does it behooves surgeons to reduce the bacterial flora of the patient's skin to as low a level as possible. This is especially true of exposed parts of the body where the resident flora may be partially composed of virulent bacteria as a result of a long contact with sources of these organisms (34). The methods of accomplishing this together with their experimental bases have been outlined by Price (33).

#### SUMMARY AND CONCLUSIONS

Infection occurs in from 3 to 5 per cent of all clean operative wounds. Barring a break in technique there are three possible sources from which the bacteria responsible for these infections may come. These are the air of the operating room, the hands of the operator and the patient's own skin. Two sources contribute to the bacteria of the air: (a) the respiratory tract of members of the operating team and (b) the skin hair and clothing of the operating team and the patient. The number of these bacteria may be reduced by measures directed toward controlling them at their source. Such measures are observance of silence and use of proper masks, wearing sterile clothing in the operating room, posturing and draping the patient before bringing him into the operating room and avoiding unnecessary motion and activity. The number of these bacteria can also be reduced by irradiating the air with ultraviolet light by spraying it with germicidal aerosols by constantly removing the contaminated air and replacing it with sterile air or by a combination of these methods. Reducing the number of bacteria in the air by irradiating the air with ultraviolet light is said by Hart (19, 20) to be accompanied by a decrease in wound infections. It has not yet been proved whether this decrease in infection is due to a decrease in the number of bacteria falling into the wound from the air to the destruction of bacteria in the wound which have gained access to it from sources other than the air, to prevention of contamination of the wound by bacteria from the adja-

cent skin, or to changes caused in the wound itself by the irradiation which make it more resistant to infection. The answer to these questions will determine the type of radiation to be used in the future.

While the number of bacteria which fall into a wound from the air is relatively small, there is evidence to prove that large numbers of bacteria may escape into a wound through holes in the surgeon's gloves. Many individuals carry virulent bacteria on their hands as well as in the nose and throat. Since the incidence of torn gloves is larger than is generally realized, the hands of the surgeon are perhaps a more dangerous source of contamination than the air. Devenish and Miles have traced an epidemic of wound infection to this source. Infection from this source can be prevented if surgeons will discard the delicate rubber gloves which tear so easily and return to the heavier ones which were worn a few decades ago.

The part played in wound contamination by the patient's own skin is uncertain. The fact that there is very little difference in the reported incidence of wound infection from clinics in which the treatment of the skin differs suggests that it is not too important. However, since it is known that the normal skin rarely harbors fewer than 10,000 bacteria per square centimeter (34), it is advisable to take all the practical steps that are available to reduce their number, at least until their significance is established. It is especially important to protect the skin during long operations for it has been shown (25) that the number of bacteria that may be recovered from the skin increases as the length of an operation increases.

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# BENEFICIAL EFFECTS OF OXYGEN THERAPY IN EXPERIMENTAL TRAUMATIC SHOCK

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**A**NOXIA is an important factor in the development of shock. A fall in blood pressure which causes a decrease in the volume and rate of blood flow through the capillaries produces stagnant anoxia. Secondary reflex and anoxic effects upon the respiratory center may produce alterations in the depth and rate of respiration and thereby cause an anoxic anoxemia. This has been demonstrated in 1920 by Aub and Cunningham. They reported that traumatic shock in cats under urethane anesthesia caused a marked slowing of the blood flow and a marked decrease in the oxygen content of the venous blood from an average of 12.3 volumes per cent to 4.8 volumes per cent. A reduction in the oxygen content of arterial blood from an average of 17.2 volumes per cent to 12.8 volumes per cent is also shown in their data.

More recently Boothby, Mayo, and Lovelace have emphasized the presence of stagnant anoxia and the need of inhalations of high oxygen concentrations in shock. They state "The blood as it passes through the capillaries gives up to the tissues, under normal circulatory conditions, only about 40 per cent of its load of oxygen. The venous blood, therefore, is still about 60 per cent saturated, and the average partial pressure of oxygen in the capillaries will correspond to approximately 35 millimeters of mercury (effect of carbon dioxide neglected). If for any reason the rate of circulation is decreased, as occurs for example in shock, the blood may give up as much as, or even more than, 80 per cent of its load of oxygen as it passes slowly through the capillaries; therefore the venous blood is only 20 per cent saturated and will exert a pressure equivalent to approximately 14 millimeters instead of 35 millimeters of mercury. Now, if nothing else is done but to cause the patient to inspire 100 per cent oxygen, instead of 21 per cent oxygen contained in the air, the arterial blood which leaves the lungs will contain, as has been shown, 2.2 cubic centimeters more oxygen per 100 cubic centimeters. In consequence the capillary and venous blood also will contain from 10 to 15 per cent more and will

be 33 per cent saturated instead of 20 per cent saturated. There will be a corresponding increase in the partial pressure of oxygen in the capillaries, from 14 to 21 millimeters, which is the equivalent of a 50 per cent increase in the pressure of oxygen in the tissues." It has been their custom to administer 100 per cent oxygen routinely to patients who have undergone extensive surgical procedures, and in the severe cases to augment this with blood transfusions.

Gellhorn and Lambert report that anoxemia produced by inhalation of 7 to 9 per cent oxygen greatly decreases the pressor reflexes of the carotid sinus in narcotized dogs. This suggests the deleterious effect of anoxemia upon this important body mechanism for maintaining the blood pressure.

Moon reports pathological evidence of disordered capillary function in the viscera and other areas remote from the site of injury in traumatic shock. He has observed capillary dilatation in the viscera, stasis, edema, and petechiae in the lungs and in the mucosa and serosa of the parenchymatous organs. Moon believes, without experimental evidence, that the presence of anoxia in shock is an important factor in producing these remote alterations in capillary permeability and tone. He logically advocates the early use of oxygen inhalations in the treatment of shock. He emphasizes his belief that the loss of body fluids in these sites remote from the injured area is of great importance in the augmentation of the shock. The local loss of body fluids into and near the traumatized area has been regarded as the most important factor in the production of experimental traumatic shock in the animal experiments of Blalock (3, 5) and of Parsons and Phemister. Blalock (4) has also observed definite alterations in the tissues of anesthetized animals subjected to traumatic shock. In some instances gross hemorrhage was seen in the lumen of the intestine. He ascribed these changes to the direct lack of sufficient oxygen. In a publication on the prevention and treatment of shock, Cressman and Blalock (7) conclude that "it would seem logical to use oxygen inhalations in the treatment of traumatic shock, at least until the blood volume could be restored, carrying the patient over a critical period."

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Increased permeability of the capillaries in the mesentery of the frog during anoxemia is reported by Landis. He found that the anoxic capillary wall failed to retain plasma proteins efficiently and the permeability to fluid was increased to 3 times normal. If the anoxemia was not too prolonged these effects on the permeability were reversible but prolonged anoxemia produced an irreversible increase in the permeability.

The importance of oxygen in maintaining capillary permeability and tone was demonstrated in the experiments of Schnedorf upon nembutal anesthetized dogs. The mild degree of trauma associated with the slow aseptic cisternal withdrawal and immediate replacement of 6 to 8 cubic centimeters of cerebrospinal fluid caused marked elevations of intracranial pressure (124 to 156 mm.) an increase in cerebrospinal fluid protein (122 mgm. per cent) and cells (1545) above normal while the arterial blood oxygen saturation was depressed 10 to 15 per cent below normal level. Similar withdrawal and replacement of cerebrospinal fluid in another series of dogs in which the blood oxygen saturation was maintained at or above normal by the administration of nasal oxygen decreased the severity of these reactions. In this group the cerebrospinal fluid pressure rose only 63 to 69 millimeters, proteins were 53 milligrams per cent and the number of cells in the cerebrospinal fluid was only 672.

The literature contains only one report of experimental studies on the effects of inhalation of high concentrations of oxygen in shock. Wood, Mason and Blalock (16) produced mild shock in 5 dogs by repeated small hemorrhage in 7 dogs by the repeated subcutaneous injection of small doses of histamine and in 11 dogs by trauma to a limb. These procedures resulted in a fall of 50 to 70 millimeters of mercury in the blood pressure, a marked increase in the pulse rate, a slowing of the respiration, an increased hematocrit volume and a low oxygen content of the blood from the femoral, renal and portal vein and from the right heart. After the dog inhaled pure oxygen for 15 minutes an average 6 and 7 millimeter rise in the blood pressure was observed in the dogs in shock produced by hemorrhage and histamine. No increase in the blood pressure of dogs in traumatic shock occurred. The pulse slowed 15 to 42 beats per minute, respirations increased 3 to 5 a minute while the oxygen content of the arterial and venous blood of the parts of the body studied was increased in all of the types of shock.

The effect of the administration of oxygen for periods longer than 15 minutes was not reported. The single observations made after 15 minutes of

oxygen do not preclude the possibility of operation during that interval of the normal body mechanisms which tend toward recovery. This possibility together with the difficulty in controlling the degree of shock and fluctuations in blood pressure by their methods warrants a further investigation of this problem.

This paper reports the results of our studies of the effect of oxygen inhalation upon experimental traumatic shock in dogs. The effects of shock due to histamine and hemorrhage will be reported separately.

#### METHOD

Twenty normal dogs were used in this study. All of the animals were deprived of food and water for 12 hours before they were used and were under basal conditions. Because of the duration of the experiments and for humane reasons the work was done under intravenous sodium pentobarbital anesthesia (25 to 30 mgm. per kilogram of body weight). Only the initial injection was necessary in all cases after the development of shock the low blood pressure helped to maintain the animal unconscious. Sodium pentobarbital anesthesia was used with a complete knowledge of its anoxic action reported by Schnedorf and also by McClure, Hartman, Schnedorf and Schelling. Even though it is responsible for some of the anoxia present in our animals it produces a basal condition in both the control and the treated animals and avoids fluctuations of the blood pressure produced by nervous and pain reflexes which would occur during manipulation of the unanesthetized dog whose limb had been traumatized.

The blood pressure and pulse rate were recorded by the optical manometric method of Hamilton et al. With this method it was not necessary to cannulate an artery. The readings were obtained by puncture of the right femoral artery with a 20 gauge needle. A record of the blood pressure, pulse and respiration was made before and every 2 hours after the trauma was produced until death occurred. The duration of life was also noted. Hematocrit determinations were made on 1 cubic centimeter samples of oxalated blood by the capillary tube method.

After the initial readings were taken an attempt was made to produce a uniform degree of trauma in all of the dogs. The left hind limb was traumatized by 20 blows to each side with an iron bar. The femur was fractured in all cases. Care was taken to confine the blows to the leg and avoid injury to the abdominal wall and main vessels. Immediately after death the intestines and viscera were examined and both lower limbs were



TABLE III — EFFECT OF OXYGEN INHALATIONS  
UPON ARTERIAL BLOOD OXYGEN IN NEM-  
BUTALIZED\* DOGS IN TRAUMATIC SHOCK

Do	Time—hrs	Atmosph oxyg ( per )						
		Blood pt	P	Res rion	H m to c l p	F m al ar r p blood		
						Cont t	L pas y	P er t ra
3			332	4		565	5	260
	3	6	3	5	660	9	33	
	6	56	8	45	90	5	875	
6			68		3	4		83
	00	06	3				33	71
		3		43	5		6	33
	7	20		56				Cl t ed
	6	00		4	53	67	3	8
		oo per cr t oxyg as l ca b (8 L per m )						
		00		4		654	65	8
			7			8		9
			60	6	3	86	6	96
	b	80	5	6	4	358		
4			4	4		35		335
			6	8		033	3	7
		00	3	8	46	43	6	9
	6	00		8		4	3006	8
s 3 m l l r m per k l r m f body w gh ve ly								

of Van Slyke and Neill. Similar analysis was made upon single samples of blood obtained from the femoral vein of 6 dogs after shock had developed.

## RESULTS AND THEIR EVALUATION

The group of 10 control and 10 treated dogs was found to be sufficiently large to cover the unavoidable variation in the degree of trauma produced by blows to the hind limb in the 2 groups of dog studied. The results presented in Tables I and II were arranged according to the increased weight of fluid loss into the traumatized limb. An average of each column is then presented at the bottom of the table. It is observed that the 2 groups of dogs were of fairly uniform weight and while the fluid weight loss into the traumatized limb expressed in percentage of the total body weight varied from 10 per cent to 59 per cent the average weight loss in the control group was 4.26 per cent and that of the group treated with oxygen was 4.11 per cent. This indicates that the average amount of trauma and fluid loss into the injured limb was fairly uniform in the 2 groups. With this in mind the difference in the length of

TABLE IV — EFFECT OF OXYGEN INHALATION  
UPON VENOUS BLOOD OXYGEN IN NEB-  
BUTALLED DOGS IN TRAUMATIC SHOCK

Dog	A month (avg. per)						
	Blood pressure	P f	Res p/r	Hemocr p	Female blood pressure		
					Content	Capacity	P
	4	2		55	80	95	7
7	39	5	5	5	37	985	9
5	60	58	38	5	66		87
A	5	40		9	960	6	6
00 pc							
	40	5			9	20 3	41
5		55		49	960	20 6	27 6
6	60		4		93	20 5	5 3
A	47	88	3		98		3
N m l y g t t f f oral l s t							
Names per dog							

life of the 2 groups of dogs is striking. The length of life of the untreated group (Table I) varied from the 3 hours and 10 minutes to 8 hours and 140 minutes averaging 4.5 hours. Dog 4 in this group lived 36 hours. This was such a wide variation from the average that it was not included in the length of life of the group. No reason can be offered for this variation except that this dog had the highest initial hematocrit reading (52 per cent) of the group and therefore may have been more resistant to shock. The length of life of the group treated with oxygen (Table II) varied from 6 hours and 45 minutes to 14 hours and 30 minutes with an average of 7 hours. This represents a 70.3 per cent increase in the duration of life over the untreated group. (Dog 4 was also omitted from this average to compensate for omission of dog 4 from the untreated group.) The average initial blood pressure fell from 135 millimeters of mercury to 64.5 millimeters of mercury in 4 hours in the untreated group while in the treated group it fell from 126.5 millimeters to only 82 millimeter of mercury. Further comparison at 6 and 8 hour intervals shows striking differences in the blood pressure and mortality in the groups. The pulse and respiration increased in both groups with the development of shock. No significant difference was observed in the averages of the group. The hematocrit determinations showed an increased concentration of the blood in both groups indicating that more plasma than red cells was lost into the traumatized limb. The average hematocrit increase in the untreated group was +6.8 per

cent and that of the untreated group was +7.5 per cent

The results of arterial blood oxygen studies upon 2 untreated and 2 treated dogs are shown in Table III. The oxygen content was low in all 4 animals (15.65 to 17.55 volumes per cent). In most instances the oxygen capacity increased with the hematocrit values. The oxygen saturation in the 2 untreated dogs increased from a low of 73 and 76 per cent before trauma to 87 and 88 per cent 6 hours after injury. The early undersaturation is due mostly to the anovemic effect of the anesthetic. However, after 4 hours the anovemia observed is caused more by the shock which is progressing and less by the anesthesia which is wearing off. In the dogs treated with oxygen the arterial oxygen saturation was maintained around 92 per cent throughout.

The normal oxygen content of blood from the femoral vein is approximately 13 to 14 volumes per cent and the oxygen saturation is about 60 per cent. Table IV shows that shock decreased the oxygen content of femoral vein blood to 5.6 volumes per cent and the saturation to 26.1 per cent. In the 3 dogs treated with oxygen inhalation the oxygen content averaged 9.8 volumes per cent and the saturation was 48.2 per cent. These results show that oxygen therapy can significantly elevate the oxygen content and saturation of the arterial and venous blood even in the presence of a slowed circulation in shock. These blood studies correlate with the more extensive observations of Aub and Cunningham and of Wood, Mason, and Blalock (16) and for this reason more studies were not made. The resistance to blood pressure fall and the increased length of life of the dogs treated with oxygen as compared with the untreated dogs demonstrates further the beneficial action of oxygen inhalation upon experimental traumatic shock.

Capillary dilatation or hemorrhage in the intestines and edema of the viscera and of the lungs, as described by Moon and Blalock (4) in their dogs, was not present in any of our animals. At autopsy the intestines were blanched, the liver and particularly the spleen were contracted suggesting loss of blood volume.

## CONCLUSIONS

1 Anoxia is very important in the development and augmentation of traumatic shock.

2 A decrease in the oxygen content and saturation of blood from the femoral artery and vein was observed in nembutalized dogs in traumatic shock. Oxygen therapy significantly increased the oxygen in the arterial and venous blood.

3 While the degree of trauma, as indicated by the average amount of fluid loss into the traumatized limb, was the same in 10 control dogs (4.26 per cent of the total body weight) and the 10 treated dogs (4.11 per cent of the total body weight) the average life of the control dogs was 4.5 hours and those treated with oxygen lived 7.7 hours. Thus the oxygen caused a 70.3 per cent increase in the duration of life in dogs with traumatic shock. The blood pressure of the dogs treated with oxygen was higher 4, 6, and 8 hours after the trauma than that of the untreated group.

4 Inhalation of a high concentration of oxygen is indicated in the treatment of traumatic shock.

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# THE TWELFTH RIB INCISION AS AN APPROACH TO THE KIDNEY

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**T**HE old popular approach to the kidney by an oblique incision 1 centimeter below the last rib has the following disabilities

1 In cases made difficult by the excessive fatness of a patient renal adhesions or other cause the exposure of the kidney may be inadequate

The subcostal nerve and its branches are liable to injury

2 The subcostal vessels or their branches and tributaries which all ramify below them must be damaged to some extent

The first disability is due to the fact that although the incision lies approximately over the middle of the kidney the upper border cannot be retracted because of the rigidity of the last rib and 1 of the fibrous structures enclosing it and continued forward from the tip (Fig 1) It has therefore been the practice to resect the last rib subperiosteally when further exposure of the kidney becomes imperative One frequently discovers however that this does not yield very much freedom because the periosteum about the rib with the subcostal vessels and nerves still forms a tight band If these have to be divided it is well to do so toward the lateral end of the rib so as to avoid danger to the pleura

It occurred to the writer that it might therefore be advantageous to make the incision directly over the last rib and carry it forward in the same line slightly higher than the usual incision After the rib has been resected the periosteum deep to it is incised longitudinally above the subcostal vessels and very far out almost at the tip In this way much freer exposure of the kidney is provided (Fig 1) and damage to subcostal vessels and nerves and their branches is avoided

Indeed as the incision is made along an intersegmental septum (between eleventh and twelfth thoracic segments) there is considerably less hemorrhage than when the incision is made lower down

Although the incision is now above the middle of the kidney the lower as well as the upper margin can be retracted sufficiently to expose the corresponding pole of the kidney as it lies in situ (Fig 1)

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The method was first practiced on a small series of cadavers and the increased freedom of exposure was remarkable It is difficult in an operative surgery class to teach the details of renal operations on a stiff formalin preserved cadaver but with the twelfth rib incision the procedures become feasible

Fear of injury to the pleura is the bugbear which might deter a surgeon from adopting the incision So far as we see this can be avoided

1 By studying an x ray film taken during extreme inspiration (Fig 2) before operation to show the exact lower limit of the pleura

2 By exposing the periosteum on the outer side of the rib before incising it prior to resection If skin muscle and periosteum are divided in one cut down to bone the knife edge might slip off the rib especially at the posterior end and open the pleura

3 By avoiding the formation of sharp projecting fragments on the stump of the last rib and covering the stump with the end of a tethered gauze roll

4 By making the longitudinal incision in the periosteum on the inner aspect of the last rib sufficiently far out to be below and beyond the pleural reflection the level of which has been shown by x ray film (Fig 2) The line of pleural reflection crosses a well formed last rib about its middle The periosteum and costal cartilage therefore are incised close to the tip of the twelfth rib and then carried on through the external and internal oblique muscles and more deeply the posterior aponeurosis of the transversus muscle The fat is then cleared away posteriorly to expose the anterior aspect of the posterior aponeurosis of the transversus muscle and it is from this aspect the kidney is first approached

As the upper pole of the kidney is being freed the upper end of the wound is stretched Some fibers of the diaphragm appearing to run laterally as well as upward may come into view at the tip of the twelfth rib and the cut started in the periosteum tears freely open along the line of the excised rib without damaging the closely adjacent and slightly adherent pleura which is pushed up without tearing

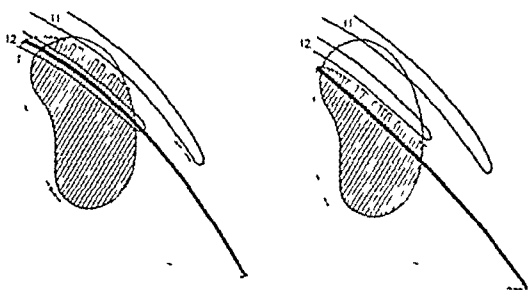


Fig 1 Diagram showing the relative areas of the left kidney which are exposed respectively by the twelfth rib incision, left, and by the subcostal incision, right

If the pleura in such a case should be torn it would not matter if (1) a close-fitting mask had been used for anesthesia so that the lung could be inflated and deflated at will, (2) the pleural rent be closed before infected matter can enter

This twelfth rib incision for kidney operations has been practiced by the author in 13 cases without accident and in all these has given unusually free exposure. These comprised 8 nephrectomies, 2 for malignant disease, 1 for branched calculus, 3 for multiple calculi, 1 for tuberculous kidney, and 1 for an enormous hydronephrosis, 4 pyelolithotomies, 1 nephrostomy with subsequent removal of calculus

The same incision is of great value in approaching the lumbar sympathetic chain, the suprarenal gland, and the greater splanchnic nerve. I have employed it in only 1 case of megacolon, but it has been employed rather extensively for these pur-

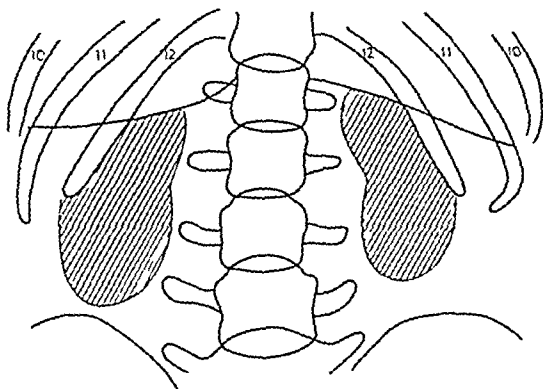


Fig 2 Tracing of a roentgenogram of the kidneys during deep inspiration. The lungs have descended to reach the line of pleural reflection which is thus rendered clearly visible

poses. The exposure of the lumbar sympathetic chain is really excellent. This same twelfth rib incision can be made use of in removing the testicular lymphatics and aortic glands in malignant disease of the testis, but it has to be supplemented of course by a separate inguinal incision, and the surgeon does not open the perirenal fascia

This twelfth rib incision<sup>1</sup> has probably been used by other surgeons for kidney operations, but this paper has been written in the belief that its advantages are not as widely appreciated as they might be

<sup>1</sup>Since writing this note the author has seen a valuable paper by E. Hess advocating resection of the twelfth rib in renal operations. *J. Urol.* 1939, 4: 943

# HORMONE STUDIES IN THE PRESENCE OF HYDATIDIFORM MOLE AND CHORIOEPITHELIOMA

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**T**HIS study was undertaken in order to determine the value of hormone analysis in the diagnosis of hydatidiform mole and chorioepithelioma. The scope of the subject necessitates its division into sections so that the hormone behavior may be considered under the following circumstances: (1) during normal pregnancy; (2) in the presence of hydatidiform mole; (3) during the interval between evacuation of the mole and the return to normal—in the event of recovery; (4) during the interval between the antecedent pregnancy and the diagnosis of malignant change—in the event of subsequent chorioepithelioma; (5) in the presence of chorioepithelioma; (6) in the event of cure or of recurrence following treatment for chorioepithelioma.

Among the several secretions that appear in increased quantities during pregnancy the chorionic hormone is of particular interest in this discussion. Under normal conditions the rise in the urinary output of this secretion has been shown by Browne and by Evans to reach tremendous proportions at about the time of the second missed menstrual period. This peak is held for a few days to be followed by a sharp drop to a moderate level which is continued throughout gestation.

By using blood serum Brindeau and Hinglais (4, 5, 6) have established standards for the prolactin content of the blood serum during the various stages of pregnancy and they have demonstrated an excessive rise in the presence of mole. Furthermore, Evans et al. found in 2 instances of normal pregnancy that the urinary peak is paralleled by that of the serum and Rakoff reached similar conclusions although his concentrations were not so high. This physiological occurrence would interfere with the correct evaluation of the hormone findings in the presence of mole and chorioepithelioma were it not for special quantitative features which are more or less characteristic of the latter conditions.

## THE HORMONE BEHAVIOR IN HYDATIDIFORM MOLE

This portion of the study is based upon 40 collected and 8 personal cases of hydatidiform mole.

In making the analysis I have included representative problems and have not listed every published report. In many instances here and elsewhere in the study the reported results have been converted into animal units per liter of fluid (urine or blood serum).

The variation in types of specimens and in test animals necessitated the preparation of several tables in order that the results may be presented with clarity. Mice and single specimens of urine were used most frequently while rats and rabbits were less often employed. The results of this technique are summarized in Table I expressed in terms of animal units per liter of fluid. When mice were used in 70 per cent the urinary prolactin concentration reached 100,000 to 800,000 mouse units per liter and in 87 per cent of the total number the prolactin elimination reached or exceeded 40,000 mouse units per liter. This constitutes the hormone picture of an active hydatidiform mole that is growing in close contact with the maternal structures. The 3 remaining cases present a different picture. The descriptions indicate that 2 of these were not productive at the time of the hormone assay. In 1 case cited by Philipp the growth was surrounded by a layer of fibrin and therefore was not in actual contact with the uterine wall. The second case was presented by Bleuler as a molar missed abortion of 14 months duration. The third case was reported by Koehler who advanced no explanation for the negative hormone tests.

Several other instances of low hormone elimination appear. At the first glance this would seem to contradict the findings in the preceding group but close analysis corrects this impression. Case 2 (F. Schultze Rhonhof) in the rat unit table shows the hormone elimination in a 9 months missed abortion of a mole. In the rabbit unit table Cases 3 and 4, reported by Schoeneck, the molar specimens were made up principally of fibrous tissue with comparatively few vesicles. Case 1 (Dabney) with a history of symptoms of 13 months duration and with uterine enlargement to the level of the umbilicus suggests a degenerating mole. The original report contained no detailed description of the mole following its evacuation. In Case 2 (Frank personal communication) a

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TABLE I — THE CONCENTRATION OF PREGNANCY PROLAN (CHORIONIC HORMONE) IN THE URINE OF 29 PATIENTS WITH HYDATIDIFORM MOLE WHOSE CASES WERE COLLECTED FROM THE LITERATURE AND BY PERSONAL COMMUNICATION

Mouse units per liter	No Cases
5 to 800,000	4
2 to 260,000	7
1 to 200,000	5
10 to 55,000	4
Negative Aschheim Zondek	3
Rat units per liter	
83,000	1
500	1
Rabbit units per liter	
16,600	1
4,760	1
500	1
200	1

single specimen of urine was titrated 24 hours after spontaneous expulsion of the mole. Any or all of 3 factors may have been responsible for the low titer: a single urine specimen, the possibility that degeneration had occurred prior to expulsion, and the fact that 24 hours had elapsed between the molar expulsion and the collection of the urine. With these logical explanations of the low titer in the atypical cases, and with the enormously high titer of prolan for those in the actively growing stage, it is apparent that the elimination of the chorionic hormone in viable molar pregnancy can be depended upon to exceed that which occurs in normal pregnancy after the third month, provided accurate quantitative determinations with 24 hour specimens of urine are made. Since the third month pregnancy peak is temporary, repeated quantitative titrations at that time will enable differentiation.

Because several workers have used blood serum, some of their results are presented in Table II

TABLE II — THE PREGNANCY PROLAN CONTENT OF THE BLOOD SERA IN 11 PATIENTS WITH HYDATIDIFORM MOLE WHOSE CASES WERE COLLECTED FROM THE LITERATURE

Rabbit units per liter	No Cases
2 to 333,000	3
1 to 200,000	2
50 to 75,000	3
20 to 25,000	2
2,000	1

Of the 11 patients in this series, 10 showed a titer of serum prolan far in excess of that seen in normal pregnancy, except at the physiological peak. In the eleventh case the test was made 24 hours after spontaneous expulsion of the mole. The workers who reported these cases used rabbits routinely (Hinglais, 7, Geurin, Valmale). By this technique — the use of blood serum and rabbits — the problem of hormone analysis in cases of suspected hydatidiform mole is reduced to the utmost simplicity, and the results justify our confidence in its diagnostic accuracy.

*Personal cases* Of 8 cases which I have studied personally, 4 exemplify the actively growing mole with greatly increased urinary prolan excretion. In all 4 a positive diagnosis was established by hormone analysis, and treatment was instituted before the passage of vesicles had occurred.

Three were studied thoroughly from the hormone point of view, both before and after eradication of the mole. The findings are summarized in Table III, which furnishes a clear-cut hormone picture of the typical molar pregnancy. The 24 hour urinary excretion of the chorionic hormone greatly exceeds that which occurs in normal pregnancy, whereas the blood serum content may reach even higher levels. The grossly normal concentration of urinary estrin is striking, and may have some diagnostic significance, particularly in making a differentiation between inevitable abortion

TABLE III — THE CONCENTRATION OF THE GONADOTROPIC AND THE ESTROGENIC HORMONES IN THE BODY FLUIDS OF 3 PATIENTS WITH ACTIVELY GROWING HYDATIDIFORM MOLE

(Personal cases)

Name	Preoperative			Postoperative			
	Urine prolan— Rab U per 24 hours	Serum prolan— Rab U per liter	Urine estrin— M U per 24 hours	Vesical fluid prolan— units per liter	Ovarian cyst fluid prolan— M U per liter	Vesical estrin—M U	Ovarian fluid estrin— M U
D W	91 000	Not done	7 40	50 000 M u	100 000	5 000	10 000
J Z	80 000	160 000	Not done	160 000 M u	Not done	Not done	Not done
R K	105 000	160 000	8 000	100 000 Rab u	Not done	Not done	Not done

Rab U rabbit units M U mouse units



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TABLE IV — THE TITERS OF THE CHORIONIC HORMONE IN 24 HOUR SPECIMENS OF URINE FROM 8 PATIENTS WITH HYDATIDIFORM MOLE

Patient	Personal cases
1 P.F.	124 000 R b
2 R.K.	108 000 R b
3 D.W.	9 000 R b
4 J.Z.	80 000 R b
5 C.I.	49 000 M
6 F.J.	500 R b
7 M.K.	23 200 R b
8 M.D.	29 gal e Fr lman

or miscarriage and hydatidiform mole Frank (15) has pointed out the sharp drop in the level of blood estrin which follows fetal death promptly, inevitable premature termination of pregnancy. I have titrated the urinary estrin and prolan in a number of inevitable miscarriages and found it much lower than the concentration found in mole or in normal pregnancy. The hormone picture of fetal death appears to be that of decreased prolan and estrin concentration in contrast to increased prolan and normal estrin in hydatidiform mole.

The hormone findings in the 8 cases of molar pregnancy that were studied personally are summarized in Table IV. The clinically typical moles were found to eliminate huge quantities of the gonadotropic hormone. The 4 remaining cases are not examples of active molar growth but serve to illustrate other phases of its existence. Case 5 (C.P.) is an example of recent degeneration followed by spontaneous expulsion of a mole. During 2 months close observation because of suspected mole the uterus rapidly increased in size suddenly to recede to three fourths its earlier dimensions. The prolan elimination at this time amounted to 48 000 mouse units in a 24 hour urinary excretion. Shortly after this a mole which was partially covered by a fibrin layer and the seat of extensive degeneration was expelled spontaneously.

TABLE VI — THE TIME REQUIRED FOLLOWING EVACUATION OF THE HYDATIDIFORM MOLE FOR THE DISAPPEARANCE OF PROLAN FROM THE URINE OF 8 PERSONAL PATIENTS WHO RECOVERED

Patient	Time required	Follow up
1 Hyst. ct my	5	2 yrs
2 Hyst. ct my	0	m
3 Hyst. ectomy	3	4 m 5.
4 Expuls n	7	3 yrs
5 Expuls n	4	mos
6 Expulsion	76	2 m 5
7 Expuls n	3	4 mos
8 Hyst rot my		m

TABLE V — THE TIME REQUIRED FOLLOWING EVACUATION OF HYDATIDIFORM MOLE FOR THE DISAPPEARANCE OF PROLAN FROM THE URINE OF 46 PATIENTS (COLLECTED FROM LITERATURE) WHO RECOVERED

Time	Cases
6 to 14 d ys	7
4 to 28 days	18
30 to 4 days	8
6 to 8 weeks	8
1 to 3 months	3
8 to 10 m nths	2
Disappeared within 8 w k	44
Disappeared within 3 m nths	2
Disappeared within 8 to 10 m nths	

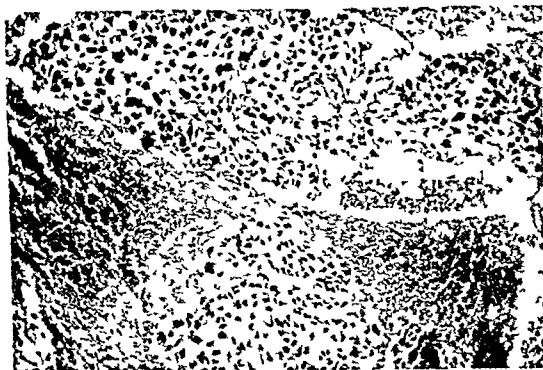
Case 6 (E.J.) shows the prolan concentration in a 24 hour specimen which was collected 24 hours after expulsion of a fibrin coated degenerated mole.

Many pathologists have observed small areas of hydatidiform degeneration in otherwise normal placentas. Similar finding with living or dead fetuses were reported recently by Masani by E Winter and by Edward Allen. Normal pregnancy with partial hydatidiform degeneration which occasioned moderately excessive prolan excretion was twice mistaken for molar pregnancy by Reeb. In Table IV patient 7 (M.K.) is a case in point with a concentration in urinary prolan of 13 200 rabbit units in 24 hours at the fourth month of pregnancy. Following hysterectomy because of an allied condition the placenta was found to contain numerous microscopic areas of molar degeneration. Since the existence of partial molar degeneration in association with living fetuses is a recognized occurrence and since the prolan concentration seems to be dependent upon both the degree of activity and the extent of the growth of the chorionic tissue the hasty acceptance of a conclusive hormone proof of complete molar degeneration should be avoided.

Several instances of missed abortion of molar pregnancy have been cited in literature an example of which is seen in Case 8 (M.D.). The patient's history included amenorrhea for 6 months with the usual symptoms of normal pregnancy during the first 3 months. Following their disappearance irregular scanty bleeding developed and persisted. Examination revealed the uterine enlargement to be the equivalent of a 2 1/2 to 3 months gestation. Without the usual signs of pregnancy. After 2 negative Friedman tests the uterus was evacuated of a mass of obviously degenerated molar tissue which was widely interspersed by fibrin.



Fig 1, left Path No 20,896  $\times 78$  Retained hydatidiform tissue removed by curettage 2 months following expulsion of a mole. Note the large pale stained chorionic villus with marked proliferation of the trophoblast b,



$\times 78$  Curettings obtained 2 months following molar expulsion containing vacuolated trophoblastic tissue. Note the irregularity in size, shape, and staining characteristics of the chorionic cells

The clinical and the hormone pictures presented by the patients herein reported and by those quoted from the literature indicate that 4 stages of activity may occur in the life history of hydatidiform mole. First is the actively growing tumor with the typical clinical signs and a tremendous prolactin concentration. The second stage occurs in the form of a minor extent of molar degeneration, often accompanying a viable fetus, with moderately excessive or normal prolactin excretion. The third form is the recently degenerated or partially encapsulated mole, with doubtful clinical criteria and a decreasing prolactin titer. The fourth stage is the missed abortion of a mole which is accompanied by a prolactin excretion that is less than that occurring in normal pregnancy. This should not result in condemnation of hormone titration as a diagnostic procedure in hydatidiform mole, but it should emphasize the importance of correlating the hormone findings and the clinical picture presented by each problem.

#### THE INTERVAL BETWEEN EVACUATION OF THE MOLE AND RECOVERY

Hormone analysis in hydatidiform mole has given rise to additional problems such as the length of time that elapses between molar evacuation and restoration to the normal hormone picture and the degree of assurance that this return offers against the likelihood of subsequent chorioepithelioma. In an attempt to solve these problems the writer has collected 46 cases from the literature and from personal communication, in addition to 8 cases that were observed personally. The wide range of this interval between the pre-existing mole and recovery is seen in Table V to extend from 6 days to 10 months. All but 5 of the cases became test-negative within 8 weeks and

only 4 per cent showed positive reactions for longer than 12 weeks. In general, the hormone level will return to normal within 3 months following the termination of molar pregnancy, but an abnormal level that persists for a longer time does not necessarily indicate the presence of chorioepithelioma, provided the level does not rise during this time.

The next question is that of the dependability of a single negative prolactin test after molar pregnancy. Such a reaction offers no assurance that the danger of chorioepithelioma has passed. The possibility that a prolonged latent period between the antecedent pregnancy and the development of chorioepithelioma may occur has been emphasized by Feiner and by others. The longest period for such latency to persist, with frequent negative

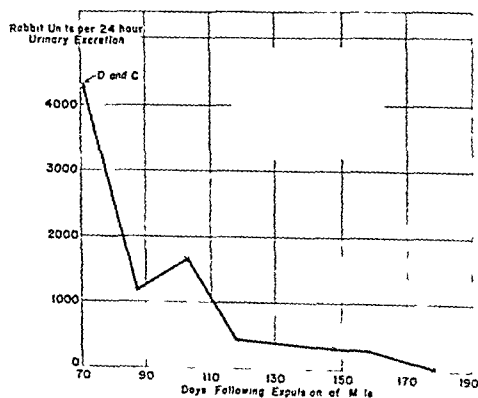


Fig 2 Case 7, M F. The concentration of the chorionic hormone 70 days following molar expulsion with the decrease in concentration subsequent to curettage until negative tests appeared 176 days after evacuation of the mole.

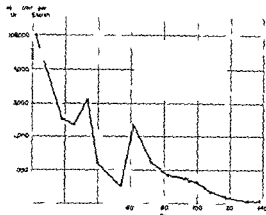


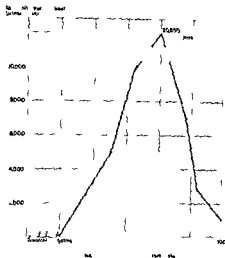
Fig 3 a l f Cas R K Showing the gradual fall in prolactin concentration of the chorionic hormone following hysterectomy and administration of mifepristone. The first negative

test has been recorded at 6 months. This interesting subject will be discussed in the section upon chorioepithelioma. For present purposes it may be stated that a follow-up period of at least 12 months after the first negative hormone test subsequent to molar pregnancy is necessary for adequate proof that malignant degeneration has not occurred.

**Personal cases.** A summary of postmolar hormone follow-up on 8 patients who have been observed personally is shown in Table 1. In the 3 instances in which hysterectomy was performed



Fig 4 Photomicrograph of chorionic villi showing the characteristic features of a molar pregnancy. The image shows a dense, cellular structure with many small, dark-staining nuclei and some larger, lighter-staining areas, characteristic of a microscopic view of a tissue sample.



test was obtained 3 days after operation. Thereafter, the prolactin level remained low and stable throughout the follow-up period of 12 months.

the time required for the disappearance of prolactin varied according to the prolactin concentration at the time of operation. A similar ratio is seen in the 3 cases of spontaneous evacuation.

Cases 7 and 8 illustrate the fact that prolonged positive reactions without a quantitative increase in prolactin do not indicate the development of chorioepithelioma. Because of the importance of this observation a detailed account of these cases follows.

Case 7: A history of intermittent abdominal pain, nausea, vomiting, and weight loss. Physical examination revealed a slightly enlarged and soft abdomen. Laboratory studies showed a hemoglobin of 11 g/dl, a hematocrit of 35%, and a white blood cell count of 12,000/mm<sup>3</sup>. The patient underwent a hysterectomy and a salpingo-oophorectomy. The gross specimen weighed 150 g and contained a large, fleshy, and lobulated mass. The microscopic examination revealed a malignant tumor consisting of nests and cords of atypical epithelial cells with high mitotic activity and areas of necrosis. The tumor was staged as T<sub>1</sub>N<sub>1</sub>M<sub>0</sub>. The patient is alive and well 12 months after surgery.

In this particular case the hormonal and clinical course demonstrated the superiority of repeated quantitative prolactin analyses over the microscopic interpretation of curettings as a guide to therapy.

A subsequent physical examination 12 months after surgery revealed a normal weight and no abdominal pain. The prolactin level remained low and stable throughout the follow-up period of 12 months.

TABLE VII—TIME BETWEEN ABORTION OR MOLAR EVACUATION AND DIAGNOSIS OF CHORIOEPITHELIOMA (44 COLLECTED CASES)

Time	No Cases
6 days	2
21 to 30 days	10
5 to 7 weeks	6
8 to 10 weeks	9
3 to 6 months	8
6 to 12 months	5
20 to 30 months	3
5½ years	1
Diagnosis made within 12 months	40 (91%)

Because of irregular spotting, a dilatation and curettage were done at that time. The curettings resembled necrotic retained secundines with the exception of one small piece of tissue which looked alive, and upon section was found to consist of actively growing chorionic tissue, impelling the pathologist to suggest a hysterectomy (Fig 4). This operation was deferred because of the gradual decrease in prolan elimination. Subsequent determinations showed a persistent drop in the urinary concentration, but the reactions remained positive for a period of 130 days following the abdominal hysterotomy. Monthly tests were negative for the next 6 months, during which 5 normal menstrual periods occurred. The patient missed her next menstrual period due to a new pregnancy. The urinary concentration of prolan incident to the new pregnancy appears in Figure 3b, wherein the physiological peak with the later recession is shown.

Here again the persistence of actively growing chorionic tissue as long as 4 months after molar evacuation did not indicate that chorioepitheliomatous degeneration was in progress, as evidenced by the decrease in prolan elimination and the subsequent clinical course.

#### THE INTERVAL BETWEEN THE PRECEDING CONDITION AND THE DIAGNOSIS OF CHORIOEPITHELIOMA

While the early diagnosis of mole is highly desirable, more important is the immediate detection of chorioepithelioma. The insidious nature of this condition and the inadequacy of former diagnostic procedures often have resulted in its hopeless advancement prior to its detection (3, 9, 12, 18, 25, 35). Furthermore, the false suspicion of its presence many times has led to needless mutilation which would have been avoided by more deliberate consideration. Hence this section, which is based upon a study of 44 collected cases, is of tremendous practical interest. This interval is seen in Table VII to have varied from 6 days to 5½ years. In 91 per cent of the cases, however, the hormone diagnosis was made within 12 months. The time between hormone tests often was excessive. Many of the cases might have been diagnosed earlier by means of more frequent hormone determinations.

TABLE VIII—HORMONE TEST NEGATIVE FOLLOWING EVACUATION OF A MOLE OR ABORTION—THEN POSITIVE, TO INDICATE DEVELOPMENT OF CHORIOEPITHELIOMA INTERVALS BETWEEN NEGATIVE AND POSITIVE TESTS SHOWN

Case	Negative	Positive
1	12 days	42 days
2	10 days	49 days
3	30 days	60 days
4	11 days	58 days
5	15 days	4 months
6	4 days	5 months
7	5 years	5 yrs, 7 months

The occasional appearance of chorioepithelioma after an apparent lengthy latent period tends to confuse the picture. Four such instances are recorded in Table VII, and comprise the 9 per cent that were not diagnosed within a year of the antecedent condition. A brief consideration of these cases follows. In the patient with a 5½ years' "latent period" (Schumann), the chronology of events suggests the likelihood of a second miscarriage or of a mole, 5 years after the first with subsequent development of chorionic malignancy. In none of the 3 remaining cases were hormone tests made prior to the one that confirmed the diagnosis of chorioepithelioma. Adair, in a personal communication, cited a curettage 20 months after a molar pregnancy which revealed chorioepitheliomatous tissue. Hormone tests confirmed this finding. Mazer reported the case of a patient who, after bleeding for 22 months, for which 2 curettements and 1 radium implantation had been done, was shown by hormone study to be suffering from chorioepithelioma. The last case (Feiner) was diagnosed 30 months after a miscarriage, which had been followed, within 2 months, by 3 curettages, none of which revealed significant tissue changes. As Feiner suggests, earlier prolan determinations may have enabled a correct diagnosis before widespread metastases developed.

A single negative reaction does not justify discontinuance of the periodic tests. The truth of this statement is borne out by the occasional appearance of a negative test, to be followed by positive reactions, to indicate the development of chorioepithelioma. Seven such occurrences are tabulated in Table VIII in which the shortest interval between negative and positive reactions is 30 days while the longest interval was 7 months.

The methods of hormone analysis that were used in the diagnosis of chorioepithelioma varied considerably. In half of the cases nothing more than qualitative tests, either single or multiple,

TABLE IX—THE PROLAN CONTENT OF URINE IN 35 COLLECTED CASES OF CHORIOEPITHELIOMA EXPRESSED IN TERMS OF RAT OR MOUSE UNITS PER LITER

U	on ent pe li	mls—R es	ml— es
200 to 500 000	6	2	
50 to 100 000	3	3	
10 to 40 000	6	0	
1 to 20 000	3	1	
to 2 000	1	0	
gal test	3		

TABLE X—THE PROLAN CONCENTRATION IN THE BLOOD SERUM OF 10 COLLECTED CASES OF CHORIOEPITHELIOMA

R bbs	pe li	% cases
400 000		2
4 000		3
1 1 4 000		1
2 1 5 000		
1 1 2 000		
R	pe li	
0 0		

were made. In the remaining group quantitative determinations were conducted but in only 16 per cent was the diagnosis based upon multiple quantitative titrations that demonstrated increasing prolan values in the body fluids. Quantitative titration is the only reliable and to an early hormone diagnosis of chorioepithelioma. By this method the presence of an intervening early pregnancy may result in erroneous conclusion unless repeated quantitative determinations are conducted. The peak of hormone excretion in pregnancy is short lasting from 6 to 8 days (Evans Browne) to be followed by a rapid decrease whereas the prolan elimination in chorioepithelioma constantly increase. These facts along with a consideration of the clinical aspects of a given case should enable early accurate diagnosis of chorioepithelioma.

#### THE HORMONE BEHAVIOR IN CHORIOEPITHELIOMA

Before weighing the value of hormone studies in the presence of chorioepithelioma the uncertainty of the other diagnostic procedures should be considered. Pick is quoted as having refused to base a diagnosis of chorioepithelioma upon curettings and this refusal is in accord with the opinion of numerous American gynecological pathologists (14-26). The classically malignant growth with a luxuriant growth of cells offers few microscopic difficulties but curettings that present a borderline picture may defy the judgment of the most expert pathologist.

A second difficulty lies in the occasional failure to obtain satisfactory curettings either because of the absence of bleeding or because it is impossible to secure sufficient tissue at the time of the operation. Profound chorioepithelioma in the absence of external bleeding has been reported by Kimbrough and by Bollen and was present in one of my cases. Many instances have been cited in which curettage failed to supply enough tissue for microscopic analysis (Cosgrove, Mazer, Segmun, etc.).

Although hormone studies should not supersede other methods quantitative prolan titration is becoming recognized more and more as an invaluable adjunct to the diagnosis of chorioepithelioma. Following the work of Fels and of Rossier in 1929 the belief soon became prevalent that excessive prolan elimination was characteristic of chorioepithelioma with the minimal standard of 50 000 mouse units per liter of urine. Subsequent studies however have proved the fallacy of this standard for many instances of undoubted chorioepithelioma have occurred that showed far smaller urinary prolan content. The wide variation in prolan elimination—ranging from negative tests to 500 000 mouse units per liter—indicates the lack of a single quantitative figure that may be regarded as the standard for the hormone diagnosis of chorioepithelioma (Table IX). Such a figure is dependable only if the values are excessive and if the possibility of intervening pregnancy can be excluded (Kobak).

Of the 27 cases that were studied in which mice were used, only 52 per cent were eliminating 50 000 or more mouse units per liter and 75 per cent of those who were studied by rat titration showed a similar concentration of the chorionic secretion. Of the negative tests (Schumann's case) has been discussed. The second case was reported by Kozima who described the microscopic picture as that of atypical chorioepithelioma. The third case that of Cosgrove is not detailed. The numerous variables that may occur in making the hormone diagnosis of chorioepithelioma might lead readily to an occasional false negative test. However this should not nullify its value as a diagnostic agent but should indicate repetition of the test.

One of the variables is a related by the use of blood serum. The employment of serum does not eliminate a wide range of quantitative values as is shown in Table X in which the serum concentration of prolan varied between 1 000 and 400 000 rabbit units per liter. The obvious lack of a single

TABLE XI — CHORIOEPITHELIOMA SHOWING THE WIDE VARIATION OF THE URINARY PROLAN CONCENTRATION (PERSONAL CASES)

Case No	Titer		Remarks
	Rabbit units per 24 hours		
1	86,000	Widespread metastasis	
2	35,000	Widespread metastasis	
3	28,800	Widespread metastasis	
4	24,150	No metastasis, recovery	
5	9,650	No metastasis, recovery	
6	Negative	Urine collected immediately after operation	
	Friedman		

diagnostic hormone titer indicates the necessity for the identification of increasing prolan concentrations as evidenced by repeated quantitative determinations to be made at weekly or biweekly intervals

*Personal cases* The author has studied 5 cases of microscopically proved chorioepithelioma by hormone analysis. In all of these analyses, 24 hour specimens of urine were used, and the results were expressed in terms of rabbit units per 24 hour excretion. Three of these cases presented widespread metastases and succumbed shortly after the hormone titration, whereas the 2 remaining patients recovered (Table XI). Of the patients who recovered, Case 5 is detailed in order to illustrate the value of repeated quantitative hormone titrations, and to emphasize the fact that excessive prolan elimination is not a necessary requirement for the diagnosis of chorioepithelioma.

**CASE 5** Patient was admitted with a history of having passed a mole 6 weeks previously. Bleeding had ceased within 1 week and did not recur. Pelvic examination was essentially negative. Quantitative titration of the urinary prolan showed the following: upon admission, 5,560 rabbit units per 24 hours, 1 week later, 9,650 rabbit units in 24 hours. The diagnosis of chorioepithelioma was made and a total hysterectomy was performed. Two weeks later, a quantitative hormone titration showed 3,360 rabbit units of prolan per 24 hours. The urinary prolan gradually decreased in quantity, and disappeared 7 months following the operation. Subsequent tests have been negative, and at present the patient is in excellent condition.

Case 6 illustrates one of the difficulties to be encountered in the microscopic diagnosis of chorioepithelioma.

A supravaginal hysterectomy was performed for what was believed to be functional uterine hemorrhage. The uterus contained an area that suggested chorioepithelioma. Immediately after the operation, a specimen of urine was collected for Friedman test which was negative. Microscopic study of the suspicious area showed marked activity of the trophoblastic cells with such extensive invasion of the myometrium that a pathological diagnosis of chorioma malignum was made (Fig 5). Subsequent to the operation routine Friedman tests remained negative for 12 months and there has been no evidence of recurrence or metastasis.

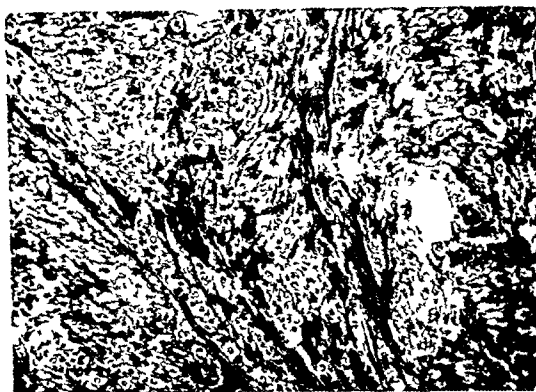


Fig 5 Path No 20,669 X78 Section from the uterine wall showing marked trophoblastic activity with infiltration of the myometrium by Langhans' and syncytial cells. No clinical or hormonal evidence of chorioepithelioma.

The author does not submit this case as one of chorioepithelioma. It is included in the group to draw attention to the fact that because of misleading microscopic pictures other uteri may have been removed needlessly, when adequate preoperative hormone study would have led to their conservation.

The successful treatment of chorioepithelioma is dependent upon its early diagnosis, which cannot be made by any isolated sign, symptom, or test. The diagnostic aids, in the order of their practical importance, are first, quantitative prolan studies, to be repeated at regular intervals; second, microscopic study of the tissues removed by curettage; third, the clinical picture presented by each doubtful case.

#### THE HORMONE PICTURE FOLLOWING TREATMENT FOR CHORIOEPITHELIOMA

Just as hormone titrations at regular intervals will permit earlier diagnoses of chorioepithelioma so will similar postoperative studies serve both as a prognostic aid and as a guide to therapy. The persistence of positive prolan tests or the subsequent development of positive reactions suggests local recurrence or distant metastases. This fact has been pointed out by Mack, Manhoff, Gertzen, and Ruzinski, each of whom reported a death from widespread chorioepithelioma in which the prolan tests either remained positive or became positive at varying intervals following operation. This observation was confirmed in 1 case in our experience.

X-ray therapy following surgical removal of chorioepithelioma is in general use and has been followed by occasional phenomenal recoveries. This form of therapy may give rise to confusing

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SURGICAL

TABLE VII--THE TIME REQUIRED FOR THE  
DISAPPEARANCE OF THE CHORIONIC HOR-  
MONE FOLLOWING TREATMENT OF CHORIO-  
EPITHELIOMA WITH RECOVERY (36 COL-  
LECTED CASES)

Cases

3

Tum	N	cs
2 to 7 d ys	3	
8 t 14 days	15	
1 t 3 d ys	8	
3 to 45 days	6	
2 t 3 m nth	2	
4 to 6 m nth		
		(66 pc e nt) 24
		(95 pc e nt) 34

hormone titrations Mack stated that temporary recession of growth with evanescent negative prolan reactions may follow roentgen ray treatment. A single negative hormone reaction following x ray therapy should not be regarded as final but the test should be repeated at monthly intervals for a year.

The question naturally arises. How soon after operation should the reactions become negative? In an attempt to answer this query, 36 records of postoperative hormone studies from known chorioepitheliomas have been collected from the literature by personal communication and through personal experience. The results of the studies are shown in Table VII from which it may be seen that the patients who recovered became test negative within 7 months. In fact 95 per cent of these patients displayed negative tests within 3 months and over two thirds of the total number were prolactin free within 30 days. The reason for the occasional long delay in the disappearance of prolactin following removal of a chorioepithelioma is not clear. The possibility of the presence of unrecognized local residual disease or of distant metastases that undergo spontaneous or postmenopausal regression must be considered. The surgical menopause or that induced by irradiation has been known to give rise to false positive pregnancy tests. Under these conditions quantitative determinations will show declining or stable levels in contrast to increasing concentrations which occur in the presence of chorioepitheliomatous activity.

SUMMARY AND CONCLUSIONS

Summary and Conclusions

The curve of prolactin concentration during normal pregnancy serves as a valuable standard for comparison in the interpretation of abnormal concentrations that are prone to occur in the presence of hydatidiform mole and chorioepithelioma.

Analyses of the clinical picture of the prolactin values and the pathological findings in hydatidiform

form mole disclose that any of 4 types of molar activity may be encountered. Since each type presents distinctive clinical and hormonal characteristics both aspects must be considered in its identification.

Following molar evacuation regularly paced hormone titrations for a year are necessary to differentiate between recovery and the development of chorioepithelioma. An increase in prolactin values denotes the presence of malignant degeneration or intervening pregnancy while a gradual decline or the lack of an increase even over a considerable period of time indicates the absence of chorioepithelioma.

In the diagnosis of chorioepithelioma repeated quantitative prolan titrations are invaluable. The final decision does not rest upon a single qualitative or quantitative determination but upon the demonstration of increased values over a short period of observation.

Following treatment for chorioepithelioma quantitative hormone studies are useful both as a prognostic aid and as a guide to subsequent treatment.

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TABLE VII—THE TIME REQUIRED FOR THE  
DISAPPEARANCE OF THE CHORIONIC HOR-  
MONE FOLLOWING TREATMENT OF CHORIO-  
EPITHELIOMA WITH RECOVERY (36 COL-  
LECTED CASES)

$T_m$	N Cases
21 7 d ys	3
8 t 4 d y	5
5 t 3 d ys	8
3 t 45 day	6
4 t 3 m ths	
4 t 6 month	

Negati	1 l ss th n 3 d y	(66 p	c nt) 4
1 l th n 3 m ths	(95 p	nt) 34	

hormone titres, he noted that temporary  
cent negat

The second is interesting because it points the way to a new method of handling the complicated problem of the partial double hare lip. By using the prolabium for the central portion of the lip in the primary repair it is possible to close the lip with far less tension and yet have the lip and vermillion border closely resemble the normal. When the child is 10 to 12 years old the prolabium can be excised and replaced by a split vermillion bordered flap from the lower lip. This adds bulk to the lip, improves the appearance of the vermillion border and deepens the sulcus between the lip and the alveolus for better fitting of a prosthesis if one is necessary. The relative fullness of the lower lip is reduced merely by the removal of the flap.

A general anesthetic is usually preferable in these cases because the patients are seldom old enough to co operate under a local nerve block. The latter method when used is safer than local infiltration because infiltration may jeopardize the blood supply of the flap. The general anesthetic can best be administered with an intra tracheal tube inserted through the mouth. A constant airway is insured and the danger of

form mole disclose that any of 4 types of molar activity may be encountered. Since each type presents distinctive clinical and hormonal characteristics, both aspects must be considered in its identification.

Following molar evacuation regularly spaced hormone titrations for a year are necessary to differentiate between recovery and the development of chorioepithelioma. An increase in protein values denotes the presence of malignant degeneration or intervening pregnancy while a gradual decline or the lack of an increase even over a considerable period of time indicates the absence of chorioepithelioma.

In the diagnosis of chorioepithelioma repeated quantitative prolan titrations are invaluable. The final decision does not rest upon a single qualitative or quantitative determination but upon the demonstration of increased values over a short time of observation.

Available treatment for chorioepithelioma consists and hormone studies are useful both as a means of diagnosis and as a guide to subsequent treatment.

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l r lps (Fg a dh) t tpe t th pp l d  
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th fl f h t l flap c t m t w d m r  
t fit th d f t p lp w ed f m th l r  
lp Th t p w jlt d g t th pl d th flap  
s t h d c th pp lp Th c ks t th p d l  
w c t d th tw l p b r s t t d (Fg d d)  
C S P t f D M S St k I t l d b  
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p lb m w thiz d f m th rml b c  
m d Th p dl f th lp as g b t th re  
lght th t th p l m (Fg d b) B se  
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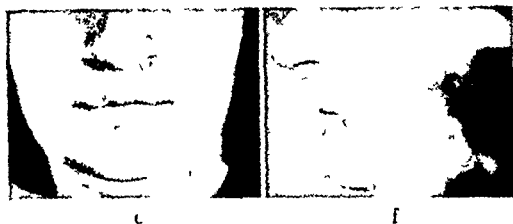
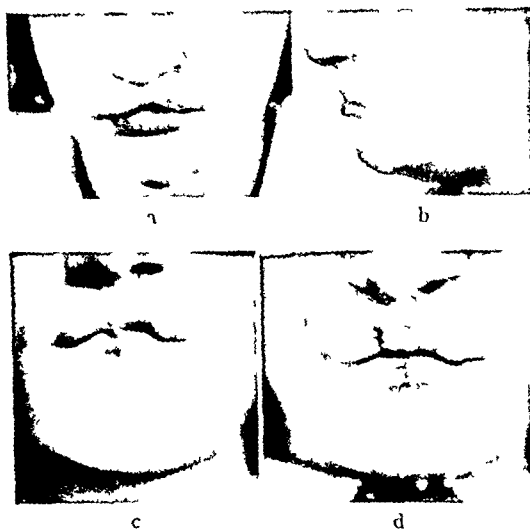


Fig 3 Illustrating the use of the split vermilion bordered flap to replace the prolabium a and b, Before operation Note the notching of the lip and the elevation of the vermilion border on the patient's left In the profile can be seen the tight upper lip, the redundant lower lip, and the rounded tip of the nose c, The intermediate stage in turning the flap, showing the pedicle intact d, Condition a few days after cutting the pedicle and adjusting the lip borders e and f, Results 2 months later The scars on the lip disappear within the floor of the nostrils The profile of the two lips is improved The tip of the nose is advanced Further correction of the nose itself will be done several years later

deficiency of tissue bulk in the prolabium At operation the prolabium and adjacent scar were excised, the incision on the left was slightly curved outward to increase the vertical length of the lip proper and thus to lower the elevated vermilion border on that side By freeing the base of the columella, the tip of the nose was advanced A split vermilion bordered flap from the lower lip was sutured into the defect (Fig 3c) Three weeks later the pedicle was cut and the borders adjusted (Fig 3, d, e and f)

#### SUMMARY

A modified vermilion bordered lip flap useful in secondary correction of the double harelip is

described and illustrated Two cases in which this procedure was used further to correct a harelip are presented

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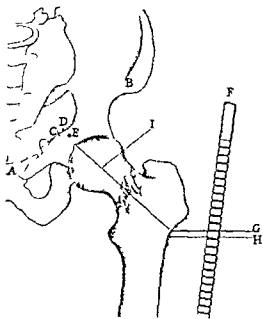


Fig 2

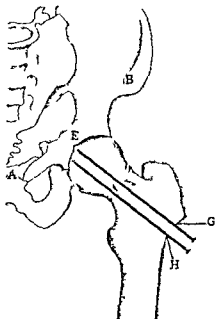
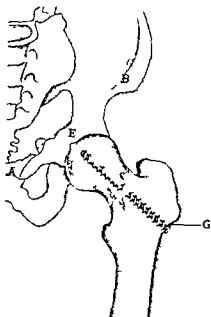
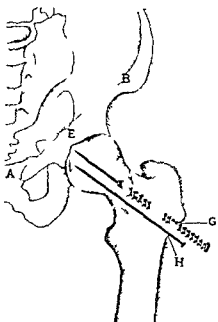


Fig 3



# MOLYBDENUM STEEL LAG SCREW IN INTERNAL FIXATION OF FRACTURED NECK OF FEMUR

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**F**RACTURE of the neck of the femur usually occurs in persons over 60 years of age. It frequently leads to many fatalities and much chronic invalidism, and may result in extensive deformity, even when considerable function has been restored. When fracture occurs at a high level, subcapital, the blood supply to the head of the femur from the neck is damaged. The supply by way of the ligamentum teres usually is inadequate. When fracture occurs at a lower level, part of the posterior capsule usually is left attached to the proximal fragment, affording it, at best, a feeble blood supply.

Since the fracture commonly occurs at an age when the cortex of the bone is thinned and its internal structure is weakened, the power of the bone repair is diminished. The more extensive the periosteal attachment to the proximal fragment, that is, the farther toward the trochanter the neck is divided, the more adequate is the blood supply and the better the chance of union. It is now recognized that even in old people there is usually an ample supply of blood to the femoral neck. Surgeons who have operated on recent fractures have seen the capsule of the joint filled with blood.

The union of these fractures is governed by hyperemic decalcification and ischemic recalcifica-

tion. When the fragments are imperfectly immobilized, movement gives rise to continued hyperemic decalcification. If there is no immobilization, this process goes on until the whole of the femoral neck has disappeared.

Plaster spica, which holds the fragments fixed to some extent but is without complete control of rotary movement, shows less degree of decalcification, nevertheless union is delayed, and if the fractures unite there is frequently a shortening of the neck.

Operative measures should secure absolute immobility. The greater percentage of fractures unite firmly without decalcification and with minimum shortening of the bone.

When the fracture is high enough to lie above all capsular attachments, the proximal fragment may be completely avascular, and in such a case there will be roentgenographic evidence later. The proximal fragment will retain its original density and will not participate in neighboring decalcification. The fact that a fracture of the femoral neck may reduce or even cut off the blood supply of the proximal fragment has important clinical applications.

The union of high cervical and subcapital fractures of the femoral neck is slow as compared with basal fractures. The impaired vascular sup-

introduction of the second Kirschner wire, to run parallel to the first wire. In order to get the proper length screw for the immobilization of the fracture, measurement is taken from the middle of the head of the femur—point *G*, immediately below the great trochanter, represented by line *I*. This measurement is superimposed upon the measuring rod and in this manner the number of quarter inches are counted on the marker, giving the correct measurement for the length of the screw necessary for the immobilization of the fracture.

Fig. 3. Two  $\frac{3}{32}$  inch Kirschner wires have been introduced in a parallel plane. *G* represents the wire in the center of the shaft of the head of the femur. *H* represents the second Kirschner wire which is  $\frac{1}{2}$  inch below the first Kirschner wire or *G*. These wires are introduced for stabilizing the fracture. *G*, the first Kirschner wire, or central wire, acts as a guide over which the screw is introduced.

Fig. 4. The 2 parallel Kirschner wires are in position and the screw is being introduced over the first Kirschner wire *G*.

Fig. 5. The screw is in position and the fragments are immobilized. The two parallel Kirschner wires, *G* and *H*, have been withdrawn.

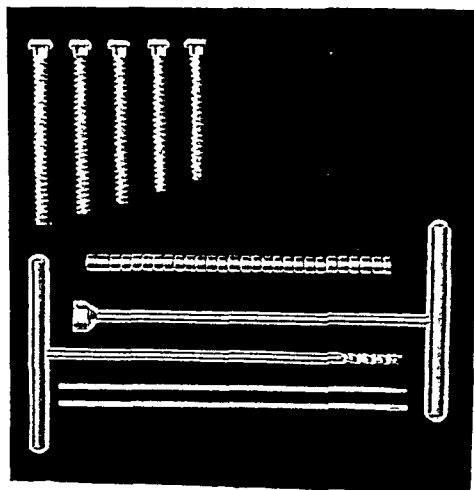
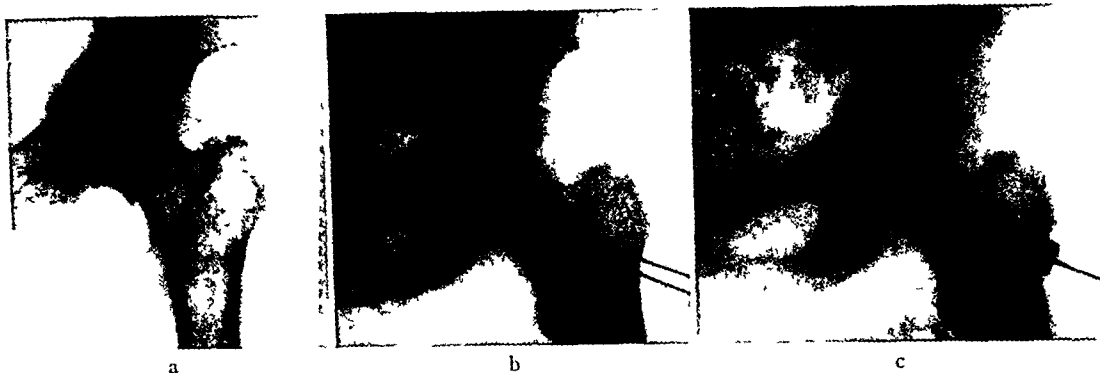


Fig. 1. Instruments required.





The danger of arthritis of the hip joint from subcapital fractures suggests that early weight bearing is inadvisable. It seems probable that weight bearing a few weeks after operation and before the fracture is united and before the cartilage has regained its blood supply will increase the tendency to degenerative bone and joint destruction.

The operation is inadvisable after the first 6 or 8 weeks in high fractures where it is probable that the blood supply of the head is impaired.

When the roentgenographs prove that the head is completely avascular the procedure is definitely contraindicated.

#### OPERATIVE TECHNIQUE

Reduction is accomplished with the use of Leadbetter's modification of the Whitman method, i.e., (1) the knee and hip are flexed to 90 degrees with traction upward, (2) internal rotation is maintained with traction and flexion, (3) the leg is brought down in measured circum-abduction and internal rotation.

The heel palm test should be applied, with the leg in abduction and internal rotation. Anteroposterior and lateral x-ray pictures should be taken to check the position of the fragments. A graduated steel marker is placed parallel to the long axis of the femur to determine the length of screw to be used.

We prefer to operate with the fractured limb in a position of flexion at the knee with extension, slight abduction, and internal rotation. To keep the patient immobilized, arm supports and well padded cross piece at the flexed knee are used, with an assistant holding the leg in abduction and internal rotation. *It is very important that the assistant carefully hold the fracture in position, as stated.*

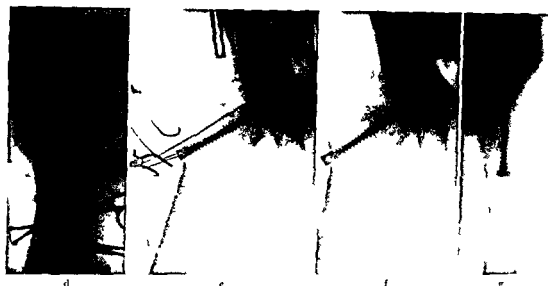
After preparation of the field, a line is drawn, gentian violet being used, from the spine of the



Fig 7 Case of Mrs. L. S., age 77, frightened by a snake, backed away suddenly and fell to ground. a, Anteroposterior view showing original fracture through neck of left femur with marker in position. b, Anteroposterior view showing Kirschner wires in position stabilizing the fracture, prior to introduction of lag screw. c, Anteroposterior view showing the lag screw being introduced over Kirschner wire of choice. d, Anteroposterior view showing screw in position with rigid coaptation of fragments. e, Lateral view showing lag screw in position. Wires removed.

pubes to the anterior superior spine of the ilium. The line is bisected. At the point of bisection the position of vein, artery, and nerve is indicated. A distance of  $\frac{1}{4}$  inch is measured out toward the crest of the ilium, and  $\frac{1}{4}$  inch below the gentian violet line a dot is made. For all practical purposes this dot represents the center of the head of the femur.

An incision is made parallel to the shaft of the femur, beginning at the lower portion of the trochanter on the lateral surface for 4 to 5 inches. All structures, i.e., skin, fascia, muscles, down to bone, are sectioned with one sweep of the knife. Towels with Michel clips or Moynihan clamps are used to block the incised skin completely. The thickness of the femur is felt between index finger and thumb. The center of shaft of femur is



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determined at the origin of the vastus externus muscle below the great trochanter. A periosteal elevator is used to reflect the attachment of the vastus externus muscle and the periosteum at this point.

A 6-inch Kirschner wire is then inserted. The point of wire is started in the middle of the femur

and directed toward the gentian violet dot keeping the drill rotating in the proper plane of the thickness of femur. The wire is introduced at the center of thickness of the femur 1/2 inch below the base of the great trochanter. The wire is introduced on a line and at the proper plane the operator should keep in mind the gentian



Fig 9. Case of Mrs. M. B. Mrs. M. B., age 71, slipped on ice, falling on left hip. a. Anteroposterior view showing original fracture of neck of left femur. b. Anteroposterior view showing reduced fracture with wire through neck of femur to act as a guide for introduction of lag screw. c. Anteroposterior view showing lag screw originally used 10 years ago in position. Note that this screw is not threaded to within  $\frac{1}{4}$  inch of the head, is in the newer type screw now being used. The old type screw proved satisfactory and was introduced in this case because no new screw of the proper length was available at the time of operation. d. Lateral view showing lag screw in position. e. Anteroposterior view taken 4 years later. Note the disappearance of the line of fracture and new trabeculae formed in the neck with complete healing of the neck. The screw is in place showing no irritation to the bone or soft parts.

violet dot marking the center of the head of the femur. One half inch below or parallel to the first wire, a second Kirschner wire is drilled into the head of the femur.

Anteroposterior and lateral x-ray pictures are then taken to check up the position of these wires. The first wire should show approximately or directly through the center of the neck and to the center or approximate center of the head of the femur. The second wire should be in a parallel position to the first wire.

When the anteroposterior and lateral x-ray pictures show that these two wires are in the proper position, a cannulated reamer slightly smaller than the caliber of the screw is inserted over the first wire or the wire which is approximately or directly in the center of the neck. The cortex of the femur is drilled. The reamer is then removed. The proper length lag screw, which length had been determined at the time the x-ray film was made with the measuring rod placed parallel to the femur, is then inserted over the first wire and inserted into the neck and head of the femur, the Kirschner wire acting as a guide in the introduction. In introducing the screw into position, the operator will notice that the threads of the screw first come in contact with the cortex of the femur. It is necessary for these screw threads to make purchase for themselves in the cortex. As soon as the distal end of the screw comes in contact with the head, it will be noticed that more purchase will be obtained and when the screw is fully introduced, the smooth or non-threaded part of the screw, which is  $\frac{1}{4}$  inch from the head, will be occupying the thickness of the

cortex of the femur, and as the screw is sent home to its position, it will draw the distal and proximal fragments together, acting not unlike a gimlet, so that the fragments at the site of the fracture will become immobilized, immobile and coapted. Both Kirschner wires are then withdrawn and the operation is completed by closure of the wound in the routine manner. The second Kirschner wire which is introduced parallel to the first wire is used as a matter of precaution, especially in subcapital fractures, so that when the screw is introduced over the top wire when it engages the distal end, the second wire acts as a stabilizer so that the head will not rotate. Anteroposterior and lateral films should then be made to recheck the position of the fragments and to complete the records.

The armamentarium necessary for this method of immobilizing fracture of the neck of the femur consists of (1) a measuring rod for determining the length of screw to be used, (2) two 6 inch Kirschner wires, (3) a reamer or drill for cutting cortex of femur over the first Kirschner wire, (4) a special wrench to fit head of lag screw, (5) the special lag screw.

The measuring rod consists of a piece of stainless steel 8 or 9 inches long, marked off in  $\frac{1}{4}$  inches. This rod is strapped parallel to the femur after reduction of the fracture. An x-ray film is taken. The distance is then measured on the x-ray film from top of head to cortex of femur. This measurement is then superimposed on the measuring rod on the same x-ray film—measuring from the top of the head to the cortex of the femur in the line in which the immobilization is



to take place—and the number of  $\frac{1}{4}$  inches are counted on measuring rod thus giving the actual length of screw to be used. It will also give the exact distance that the Kirschner wire is to be introduced.

The reamer for cutting the cortex of the femur is slightly smaller in diameter than the screw. This is threaded over the first Kirschner wire at the site that the screw is to be introduced and drilled through the cortex of the femur only. The reamer is cannulated so that it will slide over and follow the direction of the Kirschner wire.

The cannulated lag screw is hand machined from a rod of stainless steel known by trade name of 18-8 S Mo. It is very essential that the steel used in making these screws be of the finest quality. There are many kinds of stainless steel on the market. The strongest and most ductile free from oxidation and electrolysis is the metal of choice, i.e. 18 per cent chromium, 10 per cent nickel, 2.36 per cent molybdenum which is specially cold rolled and processed so as to secure maximum metallurgical properties and to all practical tests corrosion free.

This steel has the strength and ductility of vanadium steel and the added advantage of being practically non-corrosive. It is much superior to vitallium, duraluminum and monell metal all of which are objectionable—monell metal causes tissue reaction, duraluminum crystallizes in the presence of saline solutions and vitallium while non-corrosive is entirely too brittle with a tendency to the formation of air pockets in the metal as revealed in x-ray films.

The thread of this screw is a special straight thread with a depth of  $\frac{1}{16}$  in. and the thread extends from the distal end to  $\frac{1}{4}$  inch of the head. Its weight is approximately  $\frac{3}{4}$  ounce.

This lag screw serves the following purposes: (a) it immobilizes the fracture and holds the line of fracture in close coaptation so that no movements take place at the site of the fracture; (b) after the screw has immobilized the fragments it draws the fragments together and holds the fracture rigidly in anatomical position.

In accordance with this screw the bone elements adjacent to the fracture are supported and maintained in the desired position by means of a threaded screw constructed and arranged to function as an auxiliary core of the neck of the femur. The threaded portion of the screw having bearing engagement throughout a substantial area of the head and upper shaft in the region of the trochanters whereby considerable force may be exerted axially to the neck of the femur to draw the parts together.

This is a method for the reduction of the fracture of the neck of the femur which also provides an improved method of reduction and immobilization.

This method provides means of maximum support for the bone elements adjacent to the fracture.

The claims for this method of fixation are as follows:

1. A method of reducing fracture of the neck of a femur which comprises temporarily inhibiting rotative movement of the head with respect to the neck and thereafter affixing head to the neck.

2. A method of reducing fracture of the neck of the femur and fixing the fragments with two parallel  $\frac{3}{32}$  inch Kirschner wires which prevent rotation of the head with respect to the neck and of subsequently inserting the screw element over the  $\frac{3}{32}$  inch Kirschner wire which is through or approximately through the center of the neck and head in order to affix the head to the proximal end of the neck and shaft of the femur.

#### CONCLUSIONS

1. A cannulated lag screw affords maximum fixation of intertrochanteric and neck femur fractures.

The armamentarium and procedure are relatively simple and inexpensive.

3. Osteosynthesis is used for immobilization of the fragments and not for weight bearing.

4. It is important that the screw be inserted into the head to within  $\frac{1}{4}$  to  $\frac{3}{8}$  inch of the cartilage of the head of the femur.

5. Operative procedure should be deferred until the patient has recovered from shock, i.e. usually 4 to 5 days.

6. Weight bearing is contra-indicated before 5 to 6 months or until there is clinical and x-ray evidence of bony union.

During the past 10 years a series of 30 cases of fractures of the neck and intertrochanteric fractures have been operated upon. The first operation was done in 1930. Sufficient time has not yet elapsed in the majority of this series to draw definite and positive conclusions as to the final functional results.

If the lag screw is properly affixed in cases in which it is indicated it gives ample fixation. In this series only one of the screws has become loose or has been extruded. There has been no immediate operative mortality, no wound or bone infections or tissue reaction from the use of the stainless steel. Deaths occurred at later dates in senile patients from cardiac and vascular disease.

# A PERFORATED ULCER OF THE ILEUM OPPOSITE A MECKEL'S DIVERTICULUM

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and

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THE case here reported is unique in that the ulcer was situated in normal ileal mucosa opposite the stoma of a Meckel's diverticulum which was almost wholly lined with heterotopic gastric mucosa. Aschner and Karelitz report the usual position for such ulceration to be most commonly at the neck of the diverticulum or in the ileum just beyond, in which cases the diverticulum, as in our case, is almost entirely lined with heterotopic gastric mucosa. Occasionally, the ulcer is in the body of the diverticulum adjoining a patch of heterotopic gastric mucosa. These two common positions and the site for the case here reported are shown in diagram in Figure 1.

## CASE REPORT

A white male child, aged 2 years and 9 months, was admitted to the University Hospital with the chief complaint of blood in the stools. The history obtained from the parents revealed that when the youngster was about 1 year of age he awoke one night with apparently severe abdominal pain. The following day dark red, clotted blood was found in his stools. Following this the stools were tarry for several days. He was then apparently well until about 1 year later, at which time a similar episode occurred. This was again followed by a period during which the boy was quite well. Three weeks prior to the present admission, the parents again noted that the stools were dark red in color and contained a small amount of clotted blood. No abdominal pain was noticed. Three days before admission, while the patient was playing, he suddenly complained of severe abdominal pain. Soon after this his bowels moved, and again much dark red clotted blood was passed.

The family history, birth, and developmental history, and history of previous diseases were all noncontributory. There had been no epistaxis, bleeding from the gums, or petechiae. There was also no history of constipation or obstruction, nausea or vomiting.

Physical examination revealed a very pale white male child of 2½ years who appeared chronically ill, rather listless, and was not in pain. The temperature was 101.5 degrees F, rectally, the pulse, 145, and the respirations, 33 per minute. The skin was pale and had a sallow yellow tinge. The mucous membranes were very pale. The only other points of interest were limited to the abdomen. It was on a level with the thorax and was symmetrical. No rigidity or spasm was noted and no masses were felt. The

liver was hard, smooth, and the edge was 4 centimeters below the right costal margin. Rectal examination revealed no abnormality. The fecal material was light brown in color, and no blood was present on the examining glove.

The patient was admitted to the pediatrics ward for study and transfusions. The laboratory findings showed a negative blood Kahn test, negative urine, a hemoglobin of 18 per cent (Sahli), and a leucocyte count of 14,200 per cubic millimeter. A differential count showed 67 per cent polymorphonuclear cells, 33 per cent lymphocytes, and no monocytes, basophils, or eosinophils. A few nucleated red blood cells were seen. The platelets appeared slightly diminished. The red blood cells were very pale and microcytic.

The patient was given a transfusion of 175 cubic centimeters of citrated blood, and for 3 days seemed to improve. In the early morning of the fourth day the boy rather suddenly became more alert and more irritable. The temperature at this time was 101 degrees F, pulse 122 and respirations 30 per minute. The respirations increased rather rapidly to 45 per minute, the pulse to 140, the temperature to 102 degrees F. Examination showed the abdomen to be

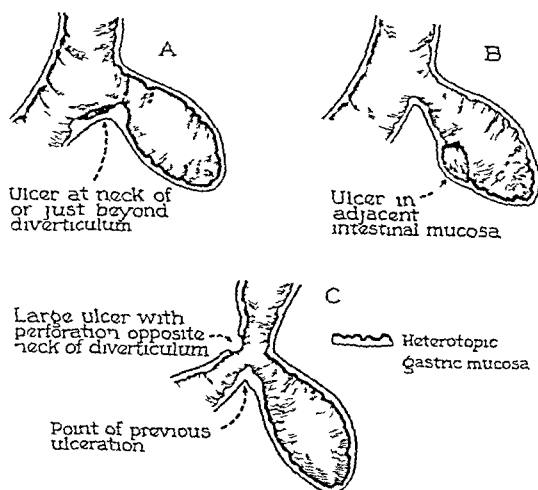


Fig. 1. A and B, Usual sites for ulcerations at Meckel's diverticula containing heterotopic gastric mucosa. C, Case reported showing ulceration and perforation opposite the stoma of a Meckel's diverticulum having a mucosa almost entirely of gastric type. The formation of pepsin and hydrochloric acid in vitelline duct remnants has been demonstrated, and the ulcerations shown are at points bearing the brunt of such an irritating secretion (Lindau and Wulff).

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Dr. Coventry now a fellow in Orthopedic Surgery, The Mayo Foundation.



Fig 2 Ext ns ep um pent um fl perf m  
t n f ul of the il mat Mckl d tucul m

d t n d t y m p n t i a d o m h a t d i f f u l y t d e  
N o b l d u n g p e r c t m o t d A t a l i b e s i  
e t e d o t u n u s h t w s p p l d t t h a b d m  
T h r e w a s o m t g d t h p t t d d o t p p e n  
e r e p L a t r n t h m r n t h e b y a b d m e n s  
t h t w t h d i s t t a n d m a k e d l y t y m p a t e  
T h e m k e d d e g o f p e m p e t e m p e s t a t t h i s  
t i m e s s h w b y t h t g e h m i l l 2 w h i c h  
w r e p o r t d a s A m t e t a c c u m u l a t n o f i r a n  
t h p e r t e l t y f l l g p e r t i f v i s c s T h e  
s t e i p e r f o t w n o t d t e r m i n d T h e w a s p e r  
t o f c d e a b l g a s i n t h e m n f t h c l N  
d m n s t a b l p e m c i f i t a t o f t h g h t l g s  
p e n t T h s t a t f t h l f l a s d e t e r m i n e  
I n c o n f e c e w t h m m b e r s f t h d p a m t f  
g r y t h d g n w m d o f p o f o t o f t h m a l l  
t e s t t h t e f a n t s c p t i r a M e k e l  
d e r t u l m

T h e l i e v e t h m r k d d s t t s m l l i b e d l e  
w a t e d t h r g h t b d m l a l l d d b l e  
g a s d p s s u r s m d i l m t h e p e n t l c t y  
N f l d w a s b t e d A l p r o t m a y t h p r f m d  
d l c a l a t h e W h t h p t o m s p e d  
a l g m o t g a d f l d e t a u n g t e c  
t d A p e r f a t n f t h s m l l i n t e t l o c t d  
w h c h b e i g d e l p e d a s f d t l t h e l t  
l m p p o t h t l M e k e l d t u c l m T h  
b w e l a t h p o t m a k d l y j c t d d m t  
B e f t h d e t l u m m p l e l f i t h p e  
f r a t a s t d e d t b e f b l d d g l y

w t h s m c h p e d s p o s b l p p o m t e l y g e t  
m t r s f t h b o w l o t a i g t h e d t u l m d t h  
p e r f r a t w r e s e c t d n d a s d t s i d e s t m  
s m d f l d w s p a t e d f m t h e p e l a d t h  
w o d w l s e d l y r t h u t d r a g D u g t h  
p t n t h p a t n t g v 3 0 0 b c t m t r s f  
c t r a t d b l o o d i t r n s l y a d o o u l c t m t r s f  
p h y s l g c l s a l s o l t O t r m f r o m t h p e r a t  
n o o o m t h b y g e l e d t p r d p t  
o f a l l u p p o t e e f f t s p a t c a s e d i h r s l t  
T h s p e c i m e n r e m e d t p e r a t o w a s f u n d t o b  
8 c t i m e t p o r t o f l m t h 3 e i m t e M k l s  
d e t u l m t t a h e d I m m d u a l l y p p o t h o p e g  
f t h d i e r t c u l m w s p e r f r a t i n t h t t l l l  
m a r i g 3 m m l m e t r s e r s e l y d 6 m m l m e t r s  
l g n t d l l y T h s o s a l s r f c o f t h b o l c  
e d b y f i b r i n p r u l t x u d t e O m c o s c p e m  
n a t n f t i e f o m t h e j u c t f t h d e t u l m t h  
t h t s t u l w l l t h e e a s f u d d e n f e a l r  
l e r a t i a s h w n b y p s u l a t d f l m t e a l t h  
f g n b o d y r t i c a t s e T h e m c o f t h e  
M e c k l d e r t c u l u m a s a l m t a n t i l y g a s t r i c t y p e  
w t h b o t h h i f n d p a r t l e l l n l g u m b e r s T h e  
i l a l m u c s a r r d g t h p r f r a t d u l e r f t h e  
o m l l l t y p e A t t p s y t h m m f i d g w a s  
e f i b r i p u r u l t p e n t o n t u s

Both the site of the ulcer in relation to the Meckel's diverticulum and the tremendous gaseous distention were unusual features in this case and they served to call attention again to the possibility of a Meckel's diverticulum being responsible for abdominal complaints. Curd in 1936 presented an excellent review of the histological material found in Meckel's diverticula. Eighty-nine collected cases contained heterotopic gastric mucosa and accounts of others containing duodenal glands, colon mucosa, and even pancreatic tissue were given. As to how these structures came to be misplaced, Curd presents the two theories: (1) The abnormal tissue represents dislocated material grafted in the vitelline duct and (2) the simpler and more obvious explanation is that the primitive endoderm, which possesses the pluripotentiality of developing into any one of the several types of epithelium or glands of the digestive tract, is stimulated locally in some undetermined manner to develop into a tissue anomalous for a particular region. Such stimulation has been thought to be irritation, inflammation, lack of bile, and relatively retarded growth at certain levels. It appears probable that any or all of these factors may be operative in variable degree.

The clinical features presented by our patient fit in well with those of the cases reviewed by Aschner and Karelitz and Brown and Pemberton. Ulcerations of a Meckel's diverticula are much more common in infants and children than in adults, and bleeding from the bowel is a regular finding, often coming in attacks associated with abdominal pain. Other than showing a marked secondary anemia, laboratory studies add

little direct information, being chiefly important in excluding blood dyscrasias and lesions of the upper and lower ends of the gastro-intestinal tract. Ulceration from a Meckel's diverticulum has potentially serious complications, 50 per cent of Aschner and Karelitz's series had perforated and produced general or local peritonitis. It is not always possible from routine studies definitely to diagnose the cause of bowel bleeding, but neither is it always safe to advise a further period of observation. From experience one should be able to make a most probable diagnosis and conclude that a laparotomy is indicated.

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## TREATMENT OF TUBERCULOUS CAVITIES

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**T**UBERCULOUS cavities are produced by the destruction of a portion of the pulmonary parenchyma and are lined with a tubercle genetic membrane which has an ever growing tendency to increase in volume. The process of pulmonary destruction can be checked only through a gradual decrease in the necrobiotic activity together with the elimination of the consequent waste products followed by the building up of a new lining of granulation tissue. The object of treatment therefore should be the cicatrization of the walls of the cavity with their contraction and reduction in size through the growth of fibrous tissue.

The inherent capacity of the peripheral tissues to contract is of the utmost importance thus attachment to neighboring solid structures such as bone or any other such obstacles prevents collapse of the cavity. The cavities usually heal rapidly after puncture of the lung nucleus as described in former papers (5 6 7). In these articles we established the fact that we have always found in the lungs of persons who have tuberculous affections in any organ of the body a specific place which shows a peculiar reaction—an area of tissue which we have named the post allergic nucleus of tuberculous focal infection. We believe that this site was formed during the period of the infection and that it has the two features which E. C. Rosenow insisted were necessary to make it a focal infection namely a capacity for elective localization by the micro-organisms and a variation in the usual form of these same micro-organisms and bacteria.

Puncture of this nucleus sets in motion a biological reaction which cleans both lungs. Then all of the infiltration exudate and waste necrobiotic tissues are reabsorbed from the cavity and neighboring structures.

Total collapse is accomplished provided the contraction capacity of the newly developed cicatricial tissue is sufficiently great and the infiltration free peripheral structures are sufficiently elastic to allow the retraction of the scar forming zone (Figs 1 2 3).

In old encapsulated cavities adherent to peripheral solid structures and adjacent to thickened pleura and especially in those cases with manifold or giant cavities we have observed that puncture seems to outline them by means of a well defined

border fibrosis. While this process appears to reduce their size it does so only on a very small scale. We also observed a thinning of the outer crusted zones perhaps because while formerly atelectatic they have now become emphysematous.

We have also occasionally noticed in patients who have been subjected to puncture of the nucleus of a tuberculous focal infection and have greatly benefited by it that if concomitantly they had one or more large cavities with thick fibrous peripheries this layer now becomes clear in the x ray picture although it has become thinner and is not continuous because of reabsorption. In them the draining bronchus is also seen well defined and dilated.

Nevertheless in monthly tomographic studies of these patients we found that the diameter of the cavities increase. We attributed this to the increased quantity of air inhaled through the dilated bronchi thus distending the recently formed fibrous tissue of the scar. It is a well known fact that precisely the opposite happens when a draining bronchus is obstructed. In the latter instance the cavity becomes smaller and collapses as has been proved both clinically and experimentally (2).

It appeared obvious therefore that in order to collapse the dilated cavity through an efficient nuclear puncture it was necessary to close its air passage. We believed that it was easier to open the cavity and close the bronchus under direct vision despite the fact that when either a tuberculous cavity or an abscess of the same origin is opened the pus drains out and a fistula is thus created.

However our wide experience in the treatment of tuberculosis of the bone has convinced us that if puncture of the postallergic nucleus of tuberculous focal infection is successfully carried out we can safely open the abscess and then close it by suture of the skin and thus attain definite healing of the operative wound by primary intention. A patient of ours was subjected to drainage of the large cavity by continuous suction (Monaldi's method) 3 months after the nucleus of his lung had been punctured. This showed that the cavity was free from exudates and necrobiotic tissue. Our operative plan was incision of the skin and thoracic aponeurosis and finally the introduction



Fig 1

Fig 2

Fig 3

Figs 1, 2, 3 Tomographic roentgenograms of A. Mart, 28 years old, taken through the chest at a level 8 centimeters from the posterior chest wall

Fig 1 Before treatment, a large cavity is shown in the right lung. All clinical symptoms indicate active tuberculosis. Koch bacilli were present in sputum.

Fig 2 Same patient, 23 days after puncture of the nucleus in the lung. Fibrosis in both lungs has begun. The

cavity is reduced. Local and general condition good. Patient has gained 4 kilograms in weight.

Fig 3 Same patient 6 months after puncture of the nucleus. The scar of the healing cavity is visible below the first rib. No Koch bacilli were isolated. Patient does not cough and has gained 5 kilograms in weight. No more symptoms of active tuberculosis. Local and general condition is splendid.

of a large sized trocar, such as an urethroscope, with a slightly sharp point which would perforate the soft perithoracic structures, an intercostal space, the pleura, and finally the lung tissue necessary to reach the cavity with the trocar. Once the trocar was within the cavity, examination could be carried out by means of an electric bulb introduced through the cannula of the trocar.

We shall now describe the technique of operation. A week before, the patient undergoes a new puncture of a lung nucleus, and 2 hours before operation, he is given an injection of morphine and scopolamine. A thorough tomographic study of the lung has already been made to determine the exact level of the cavity and whether the anterior or posterior route is the better to use. We start operation in the intercostal space nearest the cavity. This is generally the first intercostal space. The trocar is introduced with its point upward, toward the apex of the lung, the usual site of such cavities.

We generally inject novocain along the line of incision, which is about 2 centimeters long, before cutting the skin and aponeurosis. Then the anesthetist proceeds to fill the lung with oxygen under pressure so as to distend the cavity and to make it resistant to the trocar. We immediately introduce the sharp ended urethroscope through the intercostal space chosen and press it into the lung until we sense that the resistance exerted by

the pulmonary tissue has ceased. This means that the point of the instrument has entered the cavity. At this point in the procedure we ask the anesthetist to stop the administration of high pressure oxygen.

The trocar is withdrawn and an electric bulb is introduced through the cannula so that we can examine the cavity. The walls appear smooth, fibrous, are as thin and shiny as serous membrane, and contain no detritus, secretion, or exudate. In other words, they are absolutely dry. The transparency of the walls makes possible visualization of the anthracosis of the neighboring pulmonary tissue. We fix the lumen of the bronchus with the end of the cannula. A rigid swab of cotton wool, soaked in a 35 per cent solution of silver nitrate, is placed in contact with the bronchus and is left there for about 10 seconds (1). Finally the cannula is withdrawn and a stitch is placed on the skin wound. Seven days later the stitch is removed. No inflammatory reaction takes place and the wound heals permanently by primary intention—a fact which has been confirmed on examination of patients even as long as 2 years after operation.

This attained success, even when the microscopical examination of tissue from the walls of the cavity revealed the presence of tuberculous nodules, was probably due to the reduced virulence of the bacillus brought about by the beneficial humor action which followed puncture of



F 4

F 5

Fig 4 d 5 Tomog ph c tg g m f R lb C 37 years ld t k  
 thr gh th ch t t l l 6 cent m t rs f m th p t rior chest w ll  
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 rem as n th right lu g t l na d pp rs to b ry fib t d f th sam  
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 Koch bac ll p se t m sput m  
 F s s m p t t 8 m th fter ca e py Th c m h c t ed  
 P t t perit ly g d health K h b ll p se t

the post allergic nucleus of tuberculous infection Coryllos in his studie on cavernoscopy and cauterization or the use of muscle grafts says that in only 8 of 12 patients did the operative wound heal by first intention but he adds that in all of them the wound had reopened within a fortnight following the operation

The result of the inflammatory process thus provoked is the formation of abundant granulation tissue a scar which closes the bronchus This

has been confirmed by tomographic studies and repeated clinical examinations A few weeks later a still further proof may be obtained by puncturing the cavity by means of a needle attached to a syringe the sucker of which has been pushed only half way down and which through its movements will register the entrance of the point of the needle into the tuberculous cavity Withdrawal of the sucker causes a little air to enter the syringe but any further efforts in that direction will fail be cause of the negative pressure in the cavity The test proves that the lumen of the bronchus has closed

Figures 6 7 8 are from a case in which cauterization had been performed 3 months previously and perfect bronchial occlusion had been obtained as well as improvement in the patient's general condition Later however he died of pneumococcus bronchopneumonia The microscopic sections show abundant granulation tissue as a result of cauterization

During the first 2 days after operation patients complain of discomfort and dyspnea their temperature rises 1 or 2 degrees and from the third to fifth day the sputum is more or less blood stained After this stage is over the general condition of the patient steadily improves he sleeps better and his appetite is restored Roentgenograms taken 1 or 2 months later show the disappearance of exudate and the cicatrization of any remaining lung cavities We attribute this improvement to the closing of the bronchus of the large cavity and

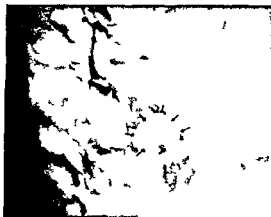


Fig 6 Postm t m an t mu alse ti f m a t be  
 cl l sc tv th l g Th rr wpo t toth c m  
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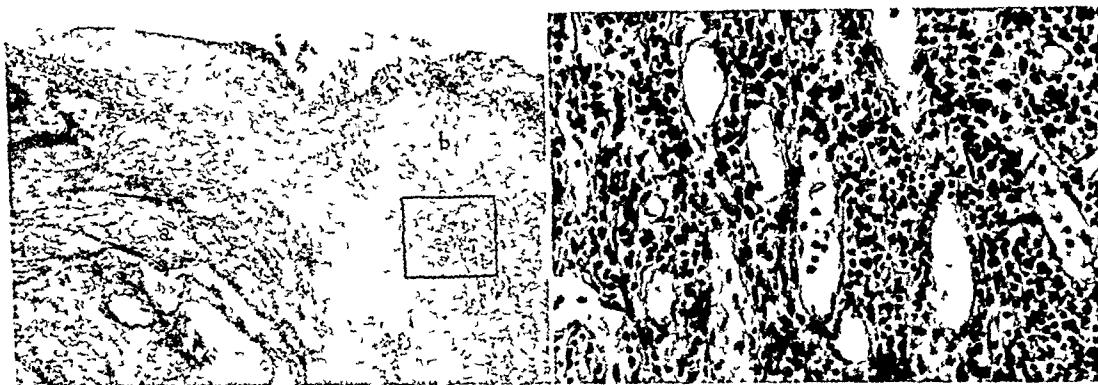


Fig 7, left Photomicrograph of a section of the same area as shown in Figure 6 a, Zone of newly formed concentric arrangement of fibrin, leucocytes, exudate b, Older zone

with newly formed capillaries, fibroblasts, plasma cells, etc

Fig 8 Photomicrograph of higher magnification of area b in Figure 7, many blood vessels, leucocytes, plasma cells

the consequent transformation of the cavity into a germ free air cyst. This process brings about general improvement in the physiological function of breathing. It is also possible that the pressure of the air which formerly reached the cavity and dilated it, aided the Koch bacillus, which requires free access to oxygen, against the beneficial humoral action set free by the puncture of the nucleus. At any rate and whatever the explanation postoperative improvement is definite and permanent.

If there are two giant cavities, each requiring the blocking of its respective draining bronchus, it is advisable to treat both in the same operation. The results in our first 2 cases led us to this conclusion, the blocking of only one bronchus was not found sufficiently beneficial on the lungs. In both of these cases fistulas developed 10 days after operation and though they closed spontaneously a few days following the cauterization of the other draining bronchus, they should always be avoided so as to prevent ulterior complications.

It must be remembered that in the presence of two large cavities a double quantity of the silver nitrate solution is required for the process of cauterization. To avoid unpleasant surprises, such as postoperative shock with great difficulty in breathing, any excess solution should be carefully removed by the proper squeezing of the cotton wool swab.

The small amount of bleeding produced when the urethroscope perforates the lung, together with the gray color of the parenchyma visible through the transparent walls of the cavity, is always remarkable. Despite the perforation, the cavity never collapses for its walls are supported by the neighboring tissue and very often by adhesions to bones.

As we have already mentioned, the perforation of the lung as a rule is bloodless, only when there are present 2 giant cavities have we found in them a little serous fluid which was removed before the bronchus was cauterized.

The air cyst, which results from the cavernoscopy and successful bronchial cauterization, generally remains as such for some time in a certain number of cases, but in others, as seen in the roentgenogram, the air is gradually reabsorbed, possibly because of the now emphysematous neighboring lung tissue. Experience has shown that the reduction in size of the cavities in the center or base of the lung is faster than elsewhere since there is a great amount of surrounding elastic tissue and since the circulating blood absorbs the air oxygen contained in the said cavities (Figs 4, 5).

We have had 4 interesting cases in which there were 2 giant cavities in the upper lobes of both lungs. Successful blocking of the draining bronchus had been carried out, although the cavities had shown only very little reduction in size. Four months later we discovered that there was an inflow of air into the cavities, this could have happened only through some unknown and undetected canal. If such an occasion arises a new cavernoscopy should be done and the guilty draining bronchus should be cauterized.

As a rule giant cavities of the apex become "clean" without reduction in size. This may be ascribed to the fact that to a large extent such cavities are enclosed in fibrous tissue which is adherent to the pleura, ribs, or vertebrae, and the small amount of lung tissue still present in the neighborhood and affected by atelectasis is not sufficient to produce function, that is, that when distended, could reduce the diameter of the cavity.



ties. Such cavities should be treated by means of plastic operations which can now be carried out under more favorable conditions for the patients thanks to our treatment for it undoubtedly excludes any possibility of a general spread of the tuberculous infection.

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# THE PERFORATION OF PANCREATIC PSEUDOCYSTS

## A Report of Six Cases

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PANCREATIC pseudocysts are not common. It may be inferred therefore, that the perforation of such a cyst would be a rarity. In the last few years, however, the authors have observed 3 such cases, which offer considerable difficulty from both the diagnostic and the therapeutic standpoint. We have found 2 other cases of perforation into the general peritoneal cavity, and 1 into the duodenum, in the records of the Cook County Hospital over a 20 year period, all of which are reported here. A review of the literature discloses that almost all textbooks on general and emergency surgery, as well as the manifold articles on pancreatic cysts, refer to the possibility of rupture of the cysts, either into the general peritoneal cavity or into a neighboring viscus. Opie quotes Schwartz as having observed a case of a pancreatic cyst in 1893, which ruptured into the general peritoneal cavity following a fall. Moynihan and Mayo-Robson in the first edition of their work on the diseases of the pancreas discuss the possibility of the rupture of the pancreatic cysts, and cite Dixon's case which was published in 1884. Bull in 1887 and Parsons in 1857 described cases of pancreatic cyst in which there was a sudden disappearance of the abdominal tumor followed by severe diarrhea. It is believed that in these cases the cyst had ruptured into the bowel at some point. Payr is quoted by Opie as having reported a case in which the tumor disappeared and reformed on 3 separate occasions at about 2 month intervals. Each disappearance of the tumor was followed by a severe diarrhea.

In more recent years, although the literature on pancreatic cysts has grown immensely, we have found but casual reference to perforation of the cysts. We have found reference but no description of the lesion in many of the texts on emergency and urgent surgery. This will attest to its rarity. The lesion is of some medicolegal importance as will be demonstrated in that 2 of our cases were "coroner's cases," and in that trauma often plays an important part, sometimes even a double rôle, as the cyst may be of traumatic

origin, and a second injury may cause rupture of the cyst.

### ETIOLOGY

In discussing the etiology of perforated pancreatic cysts, two considerations are obvious: the etiology of the cyst itself and the cause of its perforation. If trauma is involved we must decide whether the trauma has caused the original formation of the cyst, or whether the trauma is responsible for the rupture of a pre-existing cyst. We must exclude from such a discussion the simple lacerations of the pancreas, in which sufficient time has not elapsed for the formation of a pancreatic pseudocyst in which the hemorrhagic exudate bursts into the peritoneal cavity a short time after the pancreatic laceration has occurred.

As an example of such a lesion we wish to cite the case of F. P., a white boy of 9 years, who was admitted to the Cook County Hospital on August 29, 1938.

A history was given that 6 days before admission the patient had been swinging on a gate and his abdomen was crushed between this and a fence. He had been quite well except for epigastric pain and a mass which developed on the day after the injury. The parents believed that the mass was getting smaller. Physical examination revealed a fairly comfortable child, not acutely ill. A large mass was palpable in the epigastrium. On the second day after admission, the mass increased in size, and the child became acutely ill. A diagnosis of a bleeding pancreatic cyst was made and the child was operated upon. At operation a huge mass was found in the lesser peritoneal cavity containing old and fresh blood. Similar material was found in the free peritoneal cavity. About 2 liters of material was aspirated. A transfusion was administered immediately. The child appeared to be doing nicely for about 7 hours after operation, when he had a severe and uncontrollable hemorrhage from the wound, and died.

This case does not represent a true perforated pancreatic cyst, but rather a laceration of the pancreas with delayed rupture of the pancreatic hematoma.

The etiology of the pseudocyst may be, as Boyd states, either a previous attack of acute necrosis or an injury to the pancreas from trauma. The etiology of the perforation may be either trauma or, presumably, a rise in the intracystic pressure. The trauma does not necessarily cause an acute perforation at the time but may so injure the wall

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of the cyst that necrosis will occur at a subsequent time or the trauma may cause irritation of the cyst wall with further exudation and thus occasion a rise in the intracystic pressure.

In discussing unruptured pancreatic cysts Takayasu found severe abdominal trauma in 30 of 130 cases in half of which the cyst appeared within 3 months. In only 1 of our 6 cases could we consider the cyst as having been caused by injury. This patient had been struck in the epigastrium by a hard baseball 4 years before the perforation took place. One patient presumably had had an acute pancreatitis several years previously.

In 2 of the cases we believe that trauma was important in the rupture of the cyst. One patient having been kicked in the abdomen during a holdup while a second was struck in the epigastrium while sitting in the rumble seat of a car which was involved in a collision. In the 4 other cases we must presume that a rise in the intracystic pressure caused the perforation.

#### GROSS PATHOLOGY

We will not discuss the pathology of pancreatic pseudocysts. This may be found in such articles as those of Judd, Mattson and Mahorner, McWhorter et cetera. In the perforated cases we have found a small rent .05 to 1.5 centimeters in diameter in either the gastroduodenal or the gastrophrenic omentum. Although we have not seen it it is possible that the perforation may take place through the transverse mesocolon. Through these rents the contents of the pseudocyst leaked into the general peritoneal cavity, initiating a diffuse peritonitis. The cyst content was invariably a dark brown or olive viscid material containing old blood clots and partially organized material. Chemical analysis was done in 2 cases and trypsin was found in appreciable amounts. Biopsy of the cyst wall was done in 1 instance and revealed only a dense polymorphonuclear infiltration of dense connective tissue.

#### SYMPTOMS AND SIGN

It is somewhat difficult to discuss the symptoms of perforated pancreatic cysts. They fall into three groups. First there are the symptoms of the uncomplicated pancreatic cyst which may or may not be obtainable in the history. Second there are the prodromes of the actual perforation. Third there are the symptoms which attend an acute perforative peritonitis. In only 3 of the cases of this series were any symptoms obtainable suggestive of a pancreatic cyst. These patients had a vague upper abdominal distress and vomiting

for some time preceding the actual perforation. One patient stated that he had had upper abdominal distress which was occasionally relieved by taking soda while another noticed fullness in the epigastrium for the preceding several months. The prodromes to the perforation were noted in those cases in which a trauma preceded the actual perforation. These patients had severe upper abdominal distress, nausea and vomiting for several days or weeks between the time of the trauma and the actual perforation. One patient was admitted to the hospital 2 weeks before the perforation (Case 3). At this time he presented symptoms of a focalizing peritonitis in the upper abdomen which was very suggestive of an acute suppurative cholecystitis. He improved slightly under conservative management and insisted on leaving the hospital after several days but as his symptoms persisted he found it necessary to return a few hours before the perforation took place.

The history of the perforative episode was similar in all of the patients and closely resembled the anamnesis of the patient with a perforated peptic ulcer. Four of the patients felt comparatively quite well when they were suddenly seized with an excruciating upper abdominal pain. The first pain was as severe as they had ever experienced and caused the patients to double up. None of the patients fainted or felt as though they were about to faint. The pain was soon generalized over the abdomen. In none of the cases did it follow any course of spread as is so often observed in the perforation of peptic ulcers or gastric carcinoma. The pain was steady and agonizing and did not abate. All of the patients were nauseated and 4 of them vomited although only once or twice. The character of the vomitus was nondescript with the exception of 1 case in which it was described as having been black and coffee ground.

The physical examination in all of the patients was typical of a perforative peritonitis. All of the patients appeared acutely ill. The rectal temperatures varied from 97.8 to 100.6 degree, the pulse rate from 90 to 140 and the respiration from 24 to 40. The leucocyte count was elevated from 10,600 to 23,000. In all but 1 patient the positive findings were limited to the abdomen. This 1 patient had a severe mitral rheumatic heart lesion. The examination of the abdomen in each revealed a board-like rigidity. Nevertheless in 2 of the patients an upper abdominal mass could be made out. In 1 patient an upper abdominal mass which had been palpable previously had seemingly disappeared which we ascribed to the

marked muscle spasm masking the underlying tumor. Tenderness was diffuse in all of the abdomens, as was the rebound tenderness, and no localization of any kind discernible. In all but 1 patient the abdomen was completely silent, and in this instance there was some indication that the sounds were those of succussion splash. The contour of the abdomen was either flat or distended in all cases. The rectal examination was equivocal.

Serum amylase or urinary diastase tests were not done before operation in any of these patients. In 2 of the patients, blood was drawn during the operative procedure and exceedingly high values of blood amylase were found, which suggest that this test would be of great help in establishing the diagnosis.

#### DIAGNOSIS

Although a correct diagnosis was not made in this series, nevertheless, we may draw certain conclusions from a review of the case histories which may help to establish the diagnosis in future cases. A history of upper abdominal trauma, followed by a latent period, with the subsequent sudden onset of the symptoms of a perforative lesion, combined with the findings of a peritonitis and an upper abdominal mass should certainly suggest the diagnosis of a perforated pancreatic cyst. In our cases 2 were operated under the ambiguous diagnosis of "ruptured abdominal viscus," 1 as a perforated peptic ulcer, perforated gastric carcinoma, and perforated gall bladder. In 85 per cent of the cases of perforated peptic ulcer, free air will be discernible under the diaphragm. Likewise, there is usually radiation of pain toward the lower right quadrant which may also be observed in perforation of gastric tumors (4), but in the latter the pain more frequently radiates toward the left lower quadrant. Perforations of the gall bladder may be almost indistinguishable, but in the case which we had erroneously diagnosed as such, the findings in retrospect were fairly indicative of perforation of a pancreatic cyst, since the patient had a history of epigastric trauma and a palpable abdominal mass which disappeared following the onset of symptoms of peritonitis. Late or delayed ruptures of the spleen and liver may be differentiated by the profound anemia which accompanies them although 1 of our patients had a severe anemia. The rupture of the hollow viscera may be associated with the findings of free air, and often a previous history of colonic disease may be obtained, as we have reported in another communication (5). Rupture of an ectopic pregnancy may be differentiated by its typical history.

#### TREATMENT

The treatment of the perforated pancreatic cyst, of course, differs greatly from that of the unruptured one. In the former type the patient is acutely ill and often in an advanced state of surgical shock. In this series the blood pressure on admission was under 100 systolic in 3 instances. Erythrocyte counts were high in 2 cases—5,600,000 and 5,200,000, respectively. The other patients revealed a profound anemia. This would suggest that there was a definite hemoconcentration, although blood specific gravities were not carried out. It has already been noted that some of the symptoms of perforated pancreatic cyst are similar to those of an acute hemorrhagic pancreatitis, one of whose most constant symptoms is shock.

It, therefore, becomes imperative that the primary treatment be that for shock. This consists in the administration of blood, fluids, elevation of the foot of the bed, and external heat. Careful observation of the blood pressure and the blood specific gravity will reveal the patient's response to the therapy.

Operative treatment, however, appears essential. In all patients of this series an attempt was made to aspirate as much of the spilled contents of the cyst as was feasible without traumatizing the abdominal contents. In each case an attempt was then made to locate the perforation. The treatment of the cyst in this series was either packing of the cyst or actual marsupialization with packing. It appears to us, that in these seriously ill patients, the primary purpose must be to save the patient's life, wherein the eradication of the cyst is of but little importance. Therefore, the procedure which requires a minimum of manipulation and a minimum of time is the one of choice. The more active treatment of the cyst itself is a minor consideration when the mortality of the perforation is so great. This would preclude such operative procedures as excision of the cyst, or anastomosis of the cyst with the jejunum or the gall bladder, as has been suggested by Karl Meyer for nonperforated cysts.

In our opinion the best treatment is probably to bring the perforation into contact with the anterior parietal peritoneum with a few sutures and then pack the cyst with strips of iodoform gauze. This may be very difficult because of the location of the rent in the cyst, or because of the friability of the wall. If marsupialization is impossible, we suggest introducing a fenestrated rubber tube and surrounding this with strips of iodoform gauze. A Mikulicz pack with the outer gauze made of the finest mesh available might also be tried to

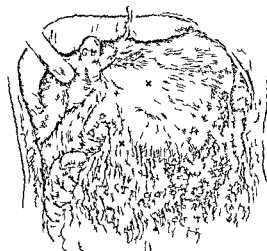


Fig. 1. Drawing illustrating the type of ruptured pancreatic pseudocyst as represented by the postoperative observation at the operating table.

advantage. Marsupialization need not be done at the site of the perforation. It should be performed at the most superficial part of the cyst and the rent closed by suture or by an omental graft. Thus if the perforation is through the gastrohepatic omentum the marsupialization can be done through the gastrocolic ligament.

The skin around the wound should then be carefully covered with a paste of aluminum paint powder to protect it from digestion by the excretions of the cyst which have in the 2 cases in which the tests were made contained pancreatic ferments in appreciable amounts. The postoperative care should be directed against surgical shock and peritonitis. We have routinely administered blood and maintained the fluid and electrolyte balance with continuous intravenous saline solution. The use of the Wangensteen method of suction for the impending paralytic ileus and the use of 100 per cent oxygen through the Boothby, Loveless and Mayo mask should help relieve distention.

#### PROGNOSIS

With the paucity of report of perforated pancreatic cysts in the literature we have been unable to determine the mortality rate in other series. In reviewing 101 operations for unruptured pancreatic cyst Osler cites 81 recoveries or a mortality of 19 per cent. Of the 6 cases in this series there were recoveries and 4 deaths or a mortality of 66 per cent. Of the 2 patients who recovered 1 (Case 4) made an absolutely uneventful

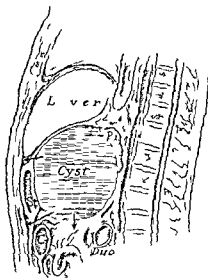


Fig. 2. Diagrammatic representation of the types of perforation of pancreatic pseudocysts.

recovery. This patient had drainage from the wound for about 3 weeks when the fistulous tract closed and has remained closed. The second patient (Case 2) that recovered developed a fecal fistula which communicated with the transverse colon. This patient had a somewhat stormy postoperative course and 2 weeks following the operation had an acute attack of epigastric pain which was associated with a marked rise in the blood amylase. This gradually subsided and the patient was discharged from the hospital 7 weeks after the operation. He returned for closure of the fecal fistula 6 months later and has been in perfect health since.

A persistent pancreatic fistula is not to be greatly feared in this type of cyst as Judd, Wattson and Mahorner have shown that in pseudocysts the absence of a lining of columnar epithelial cells permits the growth of granulation tissue and rapid obliteration of the cyst.

#### PERFORATION INTO THE BOWEL

We have been able to find but 1 example of perforation into the bowel in the files of the Cook County Hospital. In this instance the wall of the cyst was definitely malignant. The patient had a severe cardiac lesion and developed a mass in the epigastrium which was interpreted as a lobe of the liver. Shortly before death this mass receded in size. Death was not sudden but rather the patient died gradually of his cardiac decompensation.

The patient had a severe diarrhea for 2 days before death, although its significance escaped the notice of the clinicians. At autopsy a malignant cyst of the pancreas was found which had perforated into the second portion of the duodenum.

# CASE REPORTS

CASE 1. I. H., a white male of 54 years, entered the Cook County Hospital on June 30, 1937, and stated that 2 weeks previously he had been kicked in the upper abdomen. He had a pain at the time which subsided within 2 days, after which he felt comparatively well. Six days after the injury he noticed that his upper abdomen began to swell. Ten days after his injury he began to have sharp sticking pains in the upper abdomen which became more severe. On the day of admission to the hospital he had a sudden agonizing pain which was diffuse and constant. He vomited once and had a bowel movement which was said to contain gross blood. The past history was entirely negative except for a chancre in 1914.

On physical examination the patient was found to be acutely ill, to-sing about in bed and moaning with pain. The abdomen was distended to 6 centimeters above the xiphopubic line, diffusely rigid, and tender. Rebound tenderness was marked throughout. No bowel sounds were audible. The rectal examination was negative. The temperature was 98.6 degrees, pulse, 112, blood pressure, 95/60. The erythrocyte count was 1,500,000, the white count, 16,800. A diagnosis of a ruptured viscus, probably spleen, was made and operative intervention advised.

Operation was done by J. Koucky. The peritoneum contained about 5 liters of a dark brown viscid material. All peritoneal surfaces were grossly injected. No fat necrosis was observed. Behind the stomach and colon there was a huge collapsed cyst, the wall of which was about 8 millimeters thick and very tough. Brownish fluid was leaking through a 1 centimeter perforation in the gastroduodenal ligament. The perforation was surrounded by an area of necrosis 3 centimeters in diameter. The fluid in the peritoneal cavity was aspirated as well as the remaining fluid in the cyst. The wall of the cyst was then sutured to the parietal peritoneum, and the cyst was packed loosely with iodoform gauze.

The patient had a stormy postoperative course and expired on the third day after operation. A postmortem examination was made by the coroner's physician and confirmed the operative findings.

The thickness and density of the cyst wall would indicate an age much greater than 2 weeks and therefore the recent trauma was not a factor in the etiology of the cyst itself. The probable sequence of events was a traumatic necrosis of the most exposed surface of the pre-existing cyst with rupture 2 weeks later when sufficient softening of the devitalized area had occurred. Increased intracystic pressure may have contributed to the necrosis of the wall and to its ultimate rupture.

CASE 2. J. S., a white male of 49 years, was admitted to the Cook County Hospital on June 30, 1939, at 2:00 a.m. He stated that he had been in good health until 6 hours before admission. At this time he was suddenly seized with an excruciating pain which started in the epigastrium, but soon became diffuse over the abdomen. He was doubled up by the pain and was unable to move. He vomited once.

His past history was suggestive of peptic ulcer as he had dyspepsia, which was relieved somewhat by soda. He had experienced 1 attack of rather severe abdominal pain which had caused confinement to bed for 1 week, 3 years previously.

Physical examination revealed a man acutely ill, moaning with pain. The abdomen was slightly distended above the xiphopubic line, completely rigid, and diffusely tender. Rebound tenderness was marked throughout. The liver dullness was not obliterated. The rectal examination was normal. The temperature was 99.8 degrees, the pulse, 120, and the respiration, 30. The blood pressure was 90/72. The erythrocyte count was 5,600,000, the white count, 16,000. Fluoroscopy did not reveal any free air under the diaphragm. Nevertheless, a diagnosis of a perforated peptic ulcer was made, and the patient was prepared for laparotomy.

Operation was done by William Beck. The peritoneal cavity contained about 2 liters of a thick brown liquid. The gall bladder appeared normal. The duodenum was displaced downward and medially and a large mass (cyst) depressed the stomach. There was a perforation of the cyst about 1 centimeter in diameter, just above the pylorus. From this point brown liquid material poured freely. The perforation was enlarged, and the edges were sutured to the parietal peritoneum. A liberal amount of the fluid was removed for chemical and bacteriological study, and blood was drawn for a blood amylase test. The marsupialized cyst was then packed with iodoform gauze strips.

The fluid was found to contain both trypsin and amylase. The blood amylase was 124 units (normal 8-32).<sup>1</sup>

The postoperative course was stormy and the patient developed a fecal fistula connection with the transverse colon. This was subsequently closed. The patient was well when last seen 1 year after operation.

CASE 3. L. G., a Hungarian gypsy of 40 years, was first admitted to the Cook County Hospital in 1936, after having been struck in the epigastrium by a baseball. On admission he was suffering from severe epigastric pain and appeared to be in shock. After 4 days he was much improved and discharged from the hospital.

He was again admitted May 5, 1940, complaining of pain and tenderness in the abdomen which started suddenly, and remained more or less constant. At the time of this admission he had a moderate fever (varying from 99-101 degrees). He was tender in the epigastrium and had a moderate amount of rigidity. A mass was palpable in the upper abdomen which appeared to be more on the right side and was about the size of a grapefruit. It was believed that the patient either had a perigastric abscess, or an acute cholecystitis with empyema. After 4 days the patient insisted on being released from the hospital.

1 or 2 days following his release he felt quite well. Then he had a recurrence of his abdominal pain, more severe this time. He took a dose of castor oil following which he vomited several times. He, therefore, returned to the hospital and was readmitted May 12, 1940. A short time after his admission he had a sudden extremely severe pain in the epigastrium which radiated to the back. He was seen by the resident who found him gasping for breath, moaning in pain, and almost pulseless. The skin was subicteric in color and there was an icteric tint to the sclera. The abdomen was diffusely rigid and tender. Rebound tenderness was marked. The mass was no longer palpable, but it was thought that it was obscured by the rigidity. Bowel sounds were absent. The temperature was 97.8 degrees, the pulse, 112. The erythrocyte count was

<sup>1</sup>A modification of Wohlgemuth's method for blood and urine in which each unit represents the number of cubic centimeters of blood required to reduce 0.1 cubic centimeter of starch at 37 degrees C.



the mortality high—66 per cent. These and other features suggest that the diagnosis should be made as soon as possible and that operative therapy should be instituted as soon as shock is under control.

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# HOW DOES A COLOSTOMY AFFORD PROTECTION AGAINST PERITONITIS FROM SUBSEQUENT OPERATIONS

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IT is generally believed that a colostomy affords a great deal of protection against peritonitis. Just how this is obtained is not certain. There is clinical and experimental evidence to show that any abdominal operation confers on the peritoneum some degree of resistance to infection. Coller, Ransom, and Rife found that this resistance is not marked and is less than that obtained by intraperitoneal vaccination. Coller and his co-workers also found that while a colostomy in the dog affords some protection against peritonitis, the greatest degree of protection was observed after the mere subcutaneous implantation of an unopened loop of colon in which there was no factor of infection other than that incidental to an exploratory laparotomy. Their method was as follows:

The minimal lethal dose of *Bacillus coli communis* for the normal dog was determined. In their experiments this dose was found to be  $\frac{1}{2}$  of a slant of a 24-hour agar culture of *Bacillus coli communis* which contained approximately 2 billion of the organisms. An end colostomy using the distal colon was performed in healthy dogs. After 2 weeks peritonitis was produced by intraperitoneal inoculation with varying doses of colon bacillus. Of the 6 dogs, only 1 recovered and this animal had received less than the minimal lethal dose of organisms. When inoculation was delayed until one month after colostomy, no greater protection was obtained. In other experiments the following procedure was carried out:

A segment of the distal part of the colon, approximately 8 centimeters long, was drawn through the incision and implanted subcutaneously (precolostomy). Again at the end of 2 weeks peritonitis was induced by the intraperitoneal inoculation of varying doses of *Bacillus coli communis*. There was evidence of considerable protection in this group; some of the dogs surviving inoculation with 2 to 4 times the minimal lethal dose of the culture.

It has been suggested that possibly the peritoneum became immunized after a colostomy by low grade leakage around the colostomy opening. If this be true, evidence of intraperitoneal con-

tamination from the colostomy should be demonstrable with signs of peritoneal immunization as shown by an increased agglutination titre. To try to verify this, gauze constantly saturated with a 40 per cent solution of thorotrast was placed on the skin around the unopened colostomy of two patients on the second postoperative day. No evidence of intraperitoneal spread of the thorotrast was seen by roentgenogram 1 week later. While bacteria are smaller than the thorotrast particles and may have entered the peritoneal cavity, the finding noted indicates how effective and early the peritoneal seal is around the colostomy loops.

Studies were made concerning the agglutination titre of the serum against *Bacillus coli communis* in a group of patients with colonic malignancy before and after the colostomy was made. *Bacillus coli communis* was the organism tested as it is the most common bacterium found in peritonitis (Owen). The colostomies were opened on the fourth to the seventh postoperative day.

It will be seen that while there is a rise in the agglutination titre of the blood after colostomy, it tends to fall after 4 weeks (Table I). This is strikingly shown in the cases of 8 patients whose agglutination titre was studied before and then 2 and 4 weeks after colostomy (Chart 1). Of 11 patients operated upon for recurrent appendicitis, hemorrhoids, chronic cholecystitis (control), while the agglutination titre never ran as high as those after colostomy, the same phenomenon was observed. It is interesting that the agglutination titre of 10 patients studied at least 2 years after colostomy never was higher than 1:40 against *Bacillus coli communis*.

## RÉSUMÉ

From these data the protection against peritonitis afforded by colostomy is not entirely explained by peritoneal immunity alone. Undoubtedly other factors play a rôle as the formation of adhesions which limit the spread of subsequent peritonitis and the general physical improvement of the patient following colostomy. The excellent results of Jones, Rankin, and others following the one stage abdominoperineal resection for carcinoma of the rectum makes one won-

TABLE I—AGGLUTINATION TITRE OF PATIENTS' SERUM AGAINST *BACILLUS COLI COMMUNIS* FOLLOWING COLOSTOMY

Number of patients	Agglutination titre against <i>B. coli communis</i>	1st week	2nd week	4-7 weeks
Colostomy—26	Neg = 12	3	2	
	1-10 = 1	0		
	1-20 = 1	1	1	
	1-40 = 1	1		
	1-80 = 3	0	1	
	1-160 = 3	1	4	
	1-320 = 1	1	1	
	1-640 = 1	1		
	1-1280 = 2	2	1	
	1-2560 = 1	3	1	
	1-5120 = 0	3	1	

der if the protection given by a preliminary colostomy is as great as one has believed. The factors of selection of cases, care before and after operation, etc., must be taken into account, however.

It may be questioned whether the agglutination titre of the blood is comparable to that of the peritoneal fluid. There are no published studies concerning this point in the available literature. Bergen, from unpublished data concerning experimental peritonitis, believes that they are comparable. While Steinberg has never tested the agglutination titre of the peritoneal fluid against colon bacillus after injecting this organism intraperitoneally in dogs, he believes from previous experience with other antibodies and injected drugs that the peritoneal fluid has a greater concentration of these antibodies than the blood in approximately a 1:16 ratio.

It is well known that the colon bacillus is a relatively poor producer of agglutinating antibodies. The rabbit dies before an agglutination titre of any consequence can be achieved or if the animal survives the titre is not particularly high. This is also true of the dog (Steinberg).

It would seem significant that the agglutination titre was higher following colostomy than after appendectomy, cholecystectomy, and hemorrhoidectomy. However, it will be noted that 2 years after colostomy the agglutination titre of the serum was negligible against the *Bacillus coli communis*. Coller and his co-workers also found that the protection derived from laparotomy is largely lost after long periods of time.

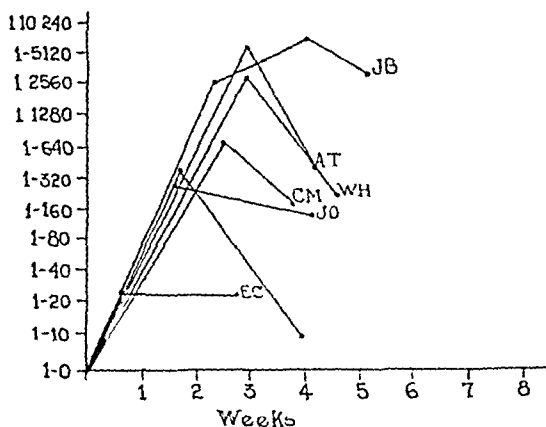


Chart 1. Agglutination titre of patients' serum against *Bacillus coli communis* following colostomy.

### CONCLUSIONS

The protection afforded by a colostomy against peritonitis is not due entirely to peritoneal "immunity," as determined by agglutination titre of the serum against the *Bacillus coli communis*. Certain physical factors secondary to the colostomy, such as intraperitoneal adhesions, general improvement of the patient, undoubtedly play a rôle.

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### LABORATORY AIDS IN SURGERY

**N**EW developments in physiological principles have contributed many times more to the progress of surgery during the past two or three decades than has progress in surgical technique itself. So often however the advantages of new physiological principles cannot be utilized without resorting to a laboratory test. This fact has led to a marked increase in cost of medical and surgical care. In view of this fact and its relationship to the possible serious detrimental social effect on the practice of medicine and in view of the added probability or certainty that hard time will follow the present world war it becomes imperative that we give serious thought to major principles in the cost of medical and surgical care. Unfortunately on many occasions the clinician hides behind the halo of the complete medical workup when in reality the patient is being exploited. Although the routine use of certain laboratory tests is to be condemned yet all will agree

that the ordinary urine and blood examinations are performed with so little time and expense and reveal so much information comparatively that they cannot be dispensed with. The purpose of this discussion is to show that many of these tests are absolutely essential to good surgical practice whereas others need be resorted to only occasionally provided sound judgment is utilized in care of the patient. It is axiomatic that as the quality of the judgment in the care of the patient decreases the more important and necessary will laboratory aids be.

There are certain tests which are so necessary in establishing a correct diagnosis that they cannot be dispensed with. For example in adenoma of the pancreas (comparatively rare) is usually associated with a fairly typical history of weakness, mental confusion, etc. alleviated by food, yet few surgeons indeed would subject a patient to a laparotomy without the confirmation of blood sugar determination and glucose tolerance test. The same could be said of the importance of blood calcium determination in the diagnosis of hyperparathyroidism. Turning to a more frequent disease I am sure that all urologists would concur in the statement that preparation of an elderly man with a long history of prostatic obstruction for suprapubic prostatectomy would be absolutely incomplete and unsafe without observations on the non-protein nitrogen level in the blood.

There are certain tests which could be used much more frequently than they are at the present time although they may be essential to the diagnosis in only the occasional case. Carcinoma of the rectum is a lesion which represents this group in so far as the data

obtained by biopsy are so conclusive. Most careful surgeons require confirmation by biopsy as a matter of routine. The surgeon who does not believe in confirmation by biopsy need make but one mistake in a decade, for example radical resection of the rectum for a benign tumor, to prove the value of biopsy confirmation. Certain patients with carcinoma of the stomach or colon may have a low blood protein because of bleeding, hepatic insufficiency, etc., and not exhibit any clinical evidence of it. Radical resection in a patient of this type may be followed by delayed healing of the anastomosed intestine, or of the wound in the abdominal wall, with consequences so serious as to cause death. A blood protein determination would detect this insufficiency, which could be corrected before operation, by transfusion of blood or plasma. Atelectasis and pneumonia are common post-operative complications. One may be mistaken for the other by the untrained clinician. When we realize that the treatment of the two lesions is so different, we can readily understand how valuable a portable roentgenogram of the chest would be, in eliminating serious consequences of ill advised therapy.

There is a large group of laboratory tests which can be omitted, by at least some surgeons, without jeopardizing the results to any significant degree. Determination of the vitamin C blood level and blood level of sulfanilamide in sulfanilamide therapy are examples of this group. It has been found recently that the blood level of sulfanilamide is not so important as it was originally thought to be. It is safe to assume that the majority of patients with a prolonged history of an inadequate and unbalanced diet accompanying carcinoma of the stomach and colon are deficient in vitamin C. The drug is so cheap that it is justifiable to omit the determination on the blood, and give it to all such patients,

along with generous quantities of orange juice. Routine daily observations on the prothrombin clotting time in obstructive jaundice no longer seems necessary. One reading just before operation should be ample to pick up the occasional patient whose prothrombin time cannot be brought to normal with the usual vitamin K therapy because of hepatic insufficiency. The point must be made however, that if scientific progress in those conditions just mentioned is to be made laboratory tests of a quantitative nature must be performed. Little may be lost therefore by decreasing the number of tests in such instances except to contribute to scientific data and progress, a privilege or obligation which unfortunately far too few accept. The routine use of a complete gastrointestinal x-ray examination and complete blood chemistry studies for every ache and pain constitutes a still greater waste of energy, time and money.

The medical profession therefore, has a responsibility of conserving not only the patient's time but also money involved in his care, regardless of whether it comes out of the pocket of the patient or from public funds. Unfortunately, it is entirely unfeasible for the doctor or an institution to make a blanket rule as to what laboratory aid should be performed on patients with a given disease. There is no substitute for the judgment and medical training required to make these decisions intelligently.

WARREN H. COLL

### HYPERACUTE PERFORATION OF THE ACUTELY INFLAMED APPENDIX

OF the 19,138 clinical records abstracted in the first Pennsylvania State-Wide Survey of acute appendicitis and its complications, none were so fact revealing as those of 70 patients admitted

with acutely inflamed intact appendices which ruptured during operation. The average age of these 70 patients was 24 years, average temperature on admission 100 degrees F, average pulse 104. The average time between onset of symptoms and operation was 48 hours. Of these 70 patients, 33 died—a mortality of 8.86 per cent. The average time between operation and death was 168 hours. This group of patients is unique not only because of the large number reported but also the definiteness of the facts regarding them.

Never before to my knowledge has it been possible to study the progress of so many patients where the period of time between perforation of the appendix and death has been accurately recorded or how and why perforation occurred and the manner in which the patients died. Some of the appendices were ruptured as delivery was almost completed, only the peritoneum adjacent to the incision becoming infected. Most of these patients recovered. The majority, however, were ruptured in the peritoneal cavity in various locations. The appendix was frequently abnormally situated and difficult to locate because of poor visibility. Without exception the peritoneum was literally prepared for the rapid absorption of toxins. I very much move of the surgeon's hand was attended by trauma or death of endothelial cells with consequent exposure of lymph and arterial capillaries.

Most of these patients developed hyperpyrexia and tachycardia almost immediately after operation. Some of them died so quickly that their abdominal walls were rigid at death. Distention, the usual accompaniment of preadmission deaths, did not have time to develop. Some of them never regained consciousness and died in a toxic delirium.

Rupture of the acutely inflamed distended appendix during operation is likely to occur because of poor relaxation of abdominal mus-

cles, inadequate exposure of the involved area, blind operating and the McBurney incision or lack of patience on the part of the surgeon.

These patients are in the excellent risk group. The majority of them therefore may be given spinal anesthesia. It is however the function of the surgeon to decide if this type of anesthesia is to be employed. The diminished excursions of the diaphragm, the decrease in the caliber of the intestine, the absence of a crowding into the wound of distended loops of intestine, all help to maintain adequate ventilation. If the anesthetist is inexperienced, open drop ether should be used. If relaxation is not satisfactory under these circumstances, the surgeon's responsibility justifies a discontinuance of the operation and a personal supervision of the administration of the anesthetic until the patient has relaxed sufficiently for him to continue.

The transverse or McBurney incision is satisfactory for removing the majority of acute appendices. If rupture of the appendix has occurred, this type of incision limits the manipulation of the operator so that a minimum of peritoneal trauma occurs with a corresponding limited absorption of bacterial toxins. It does, however, have definite disadvantages. It encourages blind operating and if enlargement of the wound is necessary, it is not as satisfactorily accomplished as with a right rectus incision.

The number of diseased appendices visualized on the opening of the peritoneum is small. Frequently loops of ileum or the cecum itself must be displaced before the appendix can be seen and invariably traction on the cecal base fails to visualize it. It is at this stage of the operation that blind surgery is most likely to be instituted. The operator inserts a finger and attempts to palpate the appendix or the process. Frequently the appendix hooks itself in the crook of the index finger—if it is a fiber

ent attempts at freeing it are made or a forceps is inserted and the base caught. This latter procedure may be safe if the wall of the appendix is thick and viable but very dangerous if the appendix is first, gangrenopurulent and distended, second, if the serous coat has ruptured and forms part of an abscess wall, and, third, if the opening has been sealed with fibrinous exudate, intestine, or omentum. An idea of how highly virulent the escaped material may be is shown by comparing the mortality of this group 82.86 per cent, with the mortality of the localizing, spreading, or abscess groups, 24.35, 24.06, and 1.2 per cent respectively. The absorbed toxins are not only more virulent but greater in amount following traumatic rupture than in any of the other in-

duced types of peritonitis. If the operator, before blindly inserting a finger, will obtain adequate exposure of the process by enlarging the incision, i.e., by splitting the sheath of the rectus and retracting the muscle fibers, or by placing a piece of sterile gauze in the transverse wound and then making a right rectus incision, these catastrophes may be avoided.

An appendix low in the pelvis, or beneath the liver or near the spleen—gangrenopurulent loaded with antigens—an inexperienced anesthetist attempting to obtain relaxation with a general anesthetic—a newly-assigned interne as an assistant—are more frequently problems of the young, than of the experienced surgeon.

JOHN O. BOWFF

# TEXTS AND DOCUMENTS

## SEVERAL MEDICAL-HISTORICAL FACTS AND ODDITIES

A B LUCKHARDT M D Chicago Illinois

THE conduct and manners of the medical profession during the greater part of the 17th and 18th centuries were decidedly different and quite if not highly objectionable to the laity and profession of the present day. In *1 Book about Doctors* Jeaffreson<sup>1</sup> has recorded a considerable amount of material concerning the life manners dress customs fees etc of the medical worthies of that period being certain to contain no line that should render it unfit for the drawing room table. Some of the medical worthies of the period of Dr William Harvey<sup>2</sup> and following it might be classed most charitably as bon vivants gourmets or gourmands. The great prevalence of gout and stone as compared with the present time is in itself indicative of the general intemperance of the period. However the point of view on such matters as food and drink was so different from the prevalent conceptions that one physician Dr Beaufoord did not refrain from expressing himself as follows - temperance (was) a vice that hadn't even the recommendation of transient pleasure (1 p 97).

The following story is told of Dr John Freind (1615-17 81).

Freind continually visited his patients in a state of intoxication. To one lady of high rank he came in such a state of confusion that when in her room he could only grumble to himself Drunk drunk drunk by God! Fortunately the fair patient was suffering

from the same malady as her doctor who (as she learned from her maid on returning to consciousness) had made the above bluff comment on her case and then had gone away. The next day Freind was sitting in a penitent state over his tea debating what apology he should offer to his aristocratic patient when he was relieved from his perplexity by the arrival of a note from the lady herself enclosing a handsome fee im-

ploring her dear Dr Freind to keep her secret and begging him to visit her during the course of the day (1 p 95).

Such examples of overindulgence with their direct deleterious effects on the stomach were probably responsible for the contrivance known as the stomach brush designed to freshen up the stomach. It was described and pictured in the *Gentleman's Magazine*<sup>3</sup> (Fig 1). The following text accompanies this cut:

Related is the execrable ventriculi or cleanser of the stomach - it is called by some of our modern physicians being composed of soft hair fastened by twisted brass or steel wire into a fasciculus as in the figure annexed the handle or stem of which may be invested with silk or thread. This instrument is recommended by several eminent physicians as being principally useful to scour or cleanse the stomach as well as

to remove foreign bodies out of the fauces and oesophagus. The brush being moistened in some convenient liquor is introduced into the oesophagus and slowly protruded in the stomach by twisting round its wire handle BB. When arrived in the stomach it is to be drawn up and down

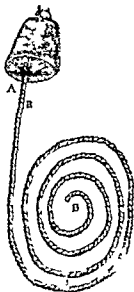


Fig 1 St m h b h d e n b e d  
n d p c t u r e d i n G e n t l e m a n M g  
1 7 5

From the Phys. Med. Lib. of the City of Chicago  
J. J. C. Jy. Jeaffreson. A Book About Doctors. London  
1781. 8 Bl. ck. tt. 5. 11. 12. 13. 14. 15. 16. 17. 18. 19. 20. 21. 22. 23. 24. 25. 26. 27. 28. 29. 30. 31. 32. 33. 34. 35. 36. 37. 38. 39. 40. 41. 42. 43. 44. 45. 46. 47. 48. 49. 50. 51. 52. 53. 54. 55. 56. 57. 58. 59. 60. 61. 62. 63. 64. 65. 66. 67. 68. 69. 70. 71. 72. 73. 74. 75. 76. 77. 78. 79. 80. 81. 82. 83. 84. 85. 86. 87. 88. 89. 90. 91. 92. 93. 94. 95. 96. 97. 98. 99. 100.

like a sucker in a syringe. But though this contrivance is greatly extolled and said to prolong life to a great age, especially if practiced once a week, month or fortnight, yet there are but very few instances of its happy effects, probably because try'd by few."

Incarcerated in the Tower of London as a political prisoner (traitor), Dr Freind planned his two volume *History of Medicine*<sup>1</sup> which is recognized as a fair presentation, though the author attempted too large a field.

In the second volume of this work occurs a discussion of the maneuver of bleeding so common from the earliest times in the treatment of diverse ailments. This discussion ends with an account of the controversy current in medical circles of the 15th century "about bleeding in the direct or the opposite side in a Pleurisy." The ridiculous seriousness of the debate, aside from the doubtful therapeutic value of the procedure, is indicated by the action of

"The University of Salamanca (which) took part with the Arabians, and made a decree, that no one in this case shou'd dare to let blood but in the contrary arm, and to add authority to their decree, they endeavour'd to procure an edict from Charles the Fifth to second it, alledging the other method to be of no less ill consequence than that of Lullier's heresy."

It may be of interest to note that while Dr Freind was in the Tower thinking of such matters and his own personal prospects, his friend Dr Richard Mead to whom he subsequently dedicated his book took care of his (Freind's) practice. On the latter's release from prison Dr Mead handed over to Freind all fees collected, which amounted to the tidy sum of 11,400 guineas (\$58,254)—surely an unusual expression of friendship and generosity. This Dr Richard Mead (1673-1754), friend of Pope, Halley and Newton, was a scholar in contrast to his predecessor Radcliffe,<sup>2</sup> who was a crude and overbearing 'bon vivant' (to put it very conservatively) with little of culture and refinement and whose secret to success as told to Mead was to "use all mankind ill."

<sup>1</sup>The History of Physick from the Time of Galen to the Beginning of the Sixteenth Century, Chiefly with Regard to Practice. In a Discourse Written to Doctor Mead by J. Freind M.D. volumes 12 mo (1st Edition, 1725) Third Edition London Printed for J. Walthoe over against the Royal Exchange in Cornhill 1727

<sup>2</sup>See A. B. Luchhardt, Surg., Gynec. & Obst., 1941 72: 674-676

Among Mead's several medical essays<sup>3</sup> there is one (p. 329) entitled "A Discourse on the Scurvy" in which after giving the symptomatology he raises the question of its etiology. Discussing the act and significance of external respiration of air in the only terms known at the time, he begins to relate scurvy in part to the noxious air which sailors are of necessity obliged to breathe during prolonged voyages. This sea air, he thinks is most certainly noxious, for

"In the first place, moisture weakens its spring (elasticity), next a combination of foul particles, such as are contained in the breath of many persons crowded together, and some perhaps diseased, then, the filthiness of water stagnating in the bottom of the ship, lastly, salts imbibed from the sea, some of which may probably have proceeded from putrefied animals in that element, may insinuate themselves into the blood and in the nature of a ferment, corrupt its whole mass."

Mead was not unconscious of the importance of the diet for he writes that some scorbutic sailors were not only relieved at St. Helena "by the fresh odoriferous air" of the island but were perfectly recovered "by eating the fruits (acidic) we have mentioned and living chiefly upon the vegetables which kind nature has supplied that place in profuse plenty." He had in a previous paragraph given evidence of the prophylactic value in sea voyages of lemons and oranges. Nevertheless he returns in the final paragraphs to the salutary effects of the land and in evidence recounts how the vapour of "the cold earth itself" contributes to the speedy recovery of those stricken with the scurvy when he writes

"Lord Anson told me that one of his men who rowed the boat ashore, was so weak, that he fell down at the oar almost dead when landed, the poor man desired his mates that they would cut a piece of turf out of the soft ground, and put his mouth to the hole upon doing this, he came to himself, and grew afterwards quite well."

Of course, the implication is that the terrestrial atmosphere was responsible for his recovery rather than an antiscorbutic diet and in the final sentence he expresses the view that a circulation of the air aboard ship "even of that which is not so wholesome" as helping much "towards the prevention of the distemper."

<sup>3</sup>The Medical Works of Richard Mead. Edinburgh Printed for Alexander Donaldson and Charles Elliot



# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

THE material in *The Role of the Liver in Surgery* by Boyce<sup>1</sup> containing of experimental work of the author and that of others in similar or allied subjects along with clinical aspects related to the experimental data represents a manuscript which was awarded the quinquennial Samuel D. Gross Prize by the Philadelphia Academy of Surgery in 1930. The contents include such subjects as liver deaths, hepatorenal syndrome, autolytic peritonitis, tests of hepatic function, hemorrhagic diathesis, therapy of hepatic insufficiency and occlusion of the portal vein. Throughout the entire book there is evidence that the experiments reported have been performed with thoroughness and exactness by one well trained in this type of work. Although the syndrome of liver death is not accepted by all the author has presented supporting data and arguments which surely would not fail to convince the most skeptical reader. The same might be said of the hepatorenal syndrome. However to the reviewer the data supporting the assumption that sudden decompression of the obstructed biliary tract may lead to serious and even fatal consequences was not conclusive perhaps the reviewer was biased by the fact that he has not been convinced that he has ever seen an instance of toxicity produced by sudden decompression of an obstructed biliary tract. The various theories offered to explain the phenomenon of fatal autolytic peritonitis (particularly in animals) is discussed in detail and a very reasonable conclusion drawn that the explanation lies in autolysis with absorption of the toxic products. Hepatic function tests are thoroughly reviewed the author concludes that dye tests, the hypuric acid test and the bilirubin test are the most sensitive. Attention is very aptly called to the fact that hepatic insufficiency may occur in patients suffering from diseases other than those of the biliary tract. The various tests for detecting prothrombin deficiency including the simple and apparently effective serum volume index test devised by the author are described. Therapy for the jaundiced patient is given in detail. The reviewer agrees wholeheartedly with the author's conclusion that routine closure of the common duct or prolonged drainage for months following cholecystectomy is unnecessary. Attention is very aptly called to the possible danger that closure of the gall bladder to save by a tight running suture following cholecystectomy may result in absorption of autolytic toxic products resulting from necrosis of strangulated liver tissue. A splendid summary of the functions of the liver is included in the appendix. The book will be extremely useful and interesting to all surgeons working in the abdominal cavity and will be a valuable addition to their library.

WARREN H. COLE

THE volume *The Pharmacological Basis of Therapeutics* by Goodman and Gilman<sup>2</sup> is a comprehensive treatise of the pharmacological actions of drugs and of their therapeutic employment. It is well documented without being tediously encyclopedic and the authors have not merely cited the literature but have appraised it. It is exceedingly well written and has evidently been prepared with great care as it is singularly free of the embarrassing errors which often occur in first editions. The material is well organized and clearly presented. There is an extensive discussion of the sulfonamide drugs of the endocrines and vitamins. This book seems destined to take a pre-eminent place in the library of the medical student and physician.

CARL A. DRASTE

IN the third edition of *Extra Ocular Muscles* Dr. Peter has made every effort to simplify the subject and facilitate the clinical study of normal and abnormal ocular motility. Heterophoria, a concomitant squint, paralytic squint, conjugate palsies and nystagmus are treated as separate phases of disturbed motility and the underlying principles are discussed. The author believes with Worth and others that fusion develops automatically with experience and practice. Early orthoptic training is stressed in the management of concomitant squint and a short chapter dealing with the essentials of orthoptic training has been added to the book.

The chapter on nystagmus has been thoroughly revised with the assistance of Dr. Joseph C. Yaskin, Professor of Neurology in the Graduate School of Medicine, University of Pennsylvania. Special attention has been given to the etiology and classification of nystagmus. Based on his conception of organic nystagmus as ocular otologic or neurologic and for the purpose of description he divides it into experimental and spontaneous types.

This book is to be recommended to all ophthalmologists and Dr. Peter can again be congratulated on his outstanding work.

JAMES C. LUNNEY

<sup>1</sup>THE ROLE OF THE LIVER IN SURGERY By Fred A. E. Sherbert, Boyce B.S. M.D. Sp. Genl. Ill. and J. Moore M.D. Charles C. Thomas

<sup>2</sup>PHARMACOLOGICAL BASIS OF THERAPEUTICS By Alfred G. Goodman and Gilman, Jr. D. Appleton-Century Co. Inc. New York, N.Y. 1935. 1112 pp. 1000 illustrations. \$10.00. 1000 illustrations. \$10.00.

# SURGERY

## GYNECOLOGY AND OBSTETRICS

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### THE HISTOLOGICAL DIAGNOSIS OF EARLY CERVICAL CARCINOMA

ROBERT MEYER, M D , Minneapolis, Minnesota

MANY of the problems involved in the diagnosis of early carcinoma of the cervix are not yet satisfactorily settled. It is urgently necessary that criteria be set down which will obviate the subjective approach to the interpretation of histologically demonstrable variations from normal. The only logical control of the correctness of such criteria lies in the observation of the clinical course of the various lesions, such studies have been carried out. It is no longer necessary to postpone a diagnosis until gross tumor is demonstrable. Experience has taught that early histological changes may now be recognized which will certainly lead on to a fatal issue in the absence of treatment. This was at the beginning, and still is, the definition of the malignancy of the tumors we call cancer.

By the same token, histological changes which may resemble those of cancer, but which are benign, may be studied by observation of the clinical course. This has also been done and these criteria recommend themselves for testing and acceptance. Close co-operation between pathologist and clinician may be expected to lead to improvement in the adequacy of the criteria for objective diagnosis.

From the Department of Obstetrics and Gynecology University of Minnesota

Charles Sumner Bacon Lecture delivered at the University of Illinois December 7 1939

The histological features of erosion healing of the cervix have been briefly discussed in a previous paper

#### LEUCOPLACIA OF THE PORTIO AND CARCINOMA

It is generally recognized that carcinoma of the cervix may arise in the presence of an old leucoplacia. Hinselmann maintains that it usually, or perhaps always, arises from leucoplacia. It must be remembered that white spots are not always leucoplacia but are often harmless and transient thickening of the superficial layers of the epithelium. Philipp followed about 80 cases showing white spots on the cervix over a long period and with repeated examinations, but was unable to demonstrate transitions to carcinoma. The author has seen only 2 cases in which early carcinoma of the portio arose from leucoplacia. These will be described below.

Figure 1 shows a section through a prominent white spot on the portio of a 41 year old woman whose complaint was irregular bleeding. The epithelium on the right, which is the white spot, shows diminution in the number of nuclei and keratinization of the superficial portion. The underlying connective tissue contains more fibrils but fewer nuclei and vessels than the more normal counterpart to the left. This represents, then, a very mild

degree of leucoplacia. Two years after biopsy the portio showed no abnormality.

#### EARLY CARCINOMA IN OLD LEUCOPLACIA

The first case was that of a 43 year old woman who had had 2 fullterm pregnancies and 1 abortion and complained of leucorrhea for many years. Multiple white spots were found on the portio and a clinical diagnosis of leucoplacia was made. The biopsy excision (Fig 2) shows a thick superficial cornified layer. The other layers are replaced by carcinoma which has also displaced the connective tissue papillae. The cornified layer being less readily digestible has been spared for the most part though in occasional areas it has been shed. The carcinoma has invaded the connective tissue in many small processes. These can be recognized in Figure 3 as made up of irregularly shaped small cells with deeply stained nuclei. There is no distinct basal layer and the abnormal cells are distributed quite irregularly in the upper layers. The row of irregular more darkly stained cells at the very surface represents the remains of the stratum granulosum. The cornified layer above this is not reproduced. Near the center may be seen 2 groups of cells with darkly stained smaller nuclei closely packed together. These cells have occupied papillae. In other portions of the material which are not illustrated here the basement membrane is still intact and sharply separates the epithelium from the connective tissue. In both positions the carcinoma is readily recognized by the atypical character of the nuclei. The carcinoma has as always started in the basal portion of the epithelium and invaded upward at the expense of the normal epithelium. The differential diagnosis is not always as simple as in this case but careful study will serve to distinguish leucoplacia from early carcinoma.

The uterus was removed 3 days after biopsy. The portio as well as the entire collum was thickened (4.5 by 5.5 centimeters). At the margin of the area excised for biopsy examination were 1 elevated small white spot and 2 flat ones. The mucosa of the external surface as well as that of the cervical canal was more white than red. The prominent spot proved similar to the biopsy specimen while

the other areas for the most part showed leucoplacia. The carcinoma then was very small and in an early stage. This finding is rare.

In the second case the portio had been treated over a long period of time with corrosives. It was finally amputated because both anterior and posterior lips were covered with white spots. The right side of the portio was somewhat thickened but flat and white. The clinical diagnosis of leucoplacia was confirmed in many areas by microscopic examination. The cornified layer was thin in most places but missing altogether in others. The squamous epithelium was thickened with irregular downgrowths.

In Figure 4 the irregularly thickened epithelium includes a papilla with a dilated vessel. On the left the basal cells are long and irregular. On the right the basal cells are also long and are connected with a small but broad downgrowth the cells of which have enlarged irregular shaped darkly stained nuclei. Near the surface the cells are regular and in the upper rows they are flat.

On both sides of a similar epithelial downgrowth in Figure 5 the basal cells of the multilayered squamous epithelium are also irregular and oblong. In the upper layer dilated vessel of the papillae may be seen. This may represent a reaction to treatment. The cell with the exception of the basal row are not strikingly changed.

A third downgrowth is seen in another area (Fig 6). This was well removed from the already described. It is surrounded by 1 or 2 rows of flat darkly stained cells which are connected with the basal cell row of the multilayered epithelium. To the right of this the basal cells are seen covering a papilla and here the basement membrane is quite indistinct. The polygonal cells above the downgrowth are irregular.

All of this is convincing evidence in support of a diagnosis of an early stage of carcinoma originating diffusely in multiple areas. For confirmation sections were examined until areas were found (Figs 7 and 8) which show epithelial invasion of lymphatics. In both areas the papillae extend for a considerable distance toward the surface. To the right in



Fig 1 Early leucoplakia of the portio Low power  
Fig 2 Early carcinoma on leucoplakia of portio  $\times 45$

Fig 3 Higher magnification of same specimen as in Figure 2  $\times 95$

Figure 7 the papillae are partly included, replaced, and displaced by the irregular downgrowths of the epithelium

In Figure 8 the epithelium surrounding the large papilla is irregular with defects in the basal membrane. On the left the epithelium appears normal with the exception of some atypical basal cells. The upper layer of flat cells is the remnant of the benign stage of the leucoplakia. The uppermost cornified layer is missing, presumably as a result of treatment. In the absence of studies of comparable cases it is impossible to determine the part which treatment may have played in the change from leucoplakia to carcinoma.

There is not, on the whole, a remarkable round cell infiltration. It is absent in the areas showing the single downgrowths (Figs 4, 5, and 6). In Figure 8 it is not striking. In Figure 7 there is a considerable infiltration of lymphocytes adjacent to the multiple downgrowths.

It is important to know that in leucoplakia, carcinoma may arise in multiple areas. Extensive histological investigation is essential under these circumstances.

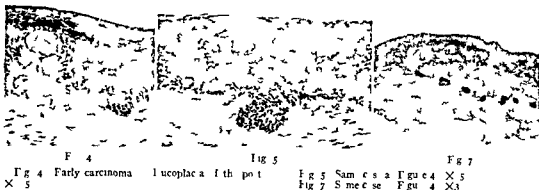
It is apparent that the first changes always take place in the basal row. The cells and the nuclei become elongated and slender. They are pressed together from side to side as a result of multiplication and are forced to extend in new directions as toward the connective tissue. The basal membrane seems to yield, not only in these areas but also in others. For example, in Figure 6 it seems to yield to the right of the connective tissue papilla. The basal membrane is fading, damaged in all

probability by the toxic influence of the carcinoma cells.

In considering the effect of multiplication of the atypical basal cells, it should be remembered that these cells may divide in one of two opposite planes. The plane of the division depends upon the axis of the mitotic spindle. If the plane of division be at a right angle or vertical to the basal membrane, the new cells lie in a plane parallel to this membrane. If the cells divide in a plane parallel to the basal membrane, the tissue becomes multilayered. It appears that oblique layering is usually the result of pressure, and it is not necessary in these circumstances to postulate an oblique position of the axis of the mitotic spindle. In cervical carcinoma, as in other similar conditions, vertical division is the earlier form. On this basis the carcinoma in Case 2 is younger carcinoma than that in Case 1, in spite of the lymphatic invasion in the former. It appears that in the second case, the carcinoma has a tendency to attain a riper form (Figs 4, 6, and 8) than in the first case.

#### THE RELATIONSHIP BETWEEN ULCERATION AND EROSION OF THE CLYVIX AND CARCINOMA

A consideration of early cervical carcinoma would be incomplete without some attention to the question of its relationship to erosion and erosion healing. A study of very early squamous cell carcinomas leads to the conclusion that they arise always from squamous epithelium and always from the basal cells. In most cases the carcinoma arises at the margin of an old erosion. The author has seen only 1 case of a very small squamous cell



carcinoma which seemed to arise within an erosion. This is not adequate proof of origin in the erosion area. Such a tumor may have spread to the erosion surface from adjacent surfaces and inflammatory reaction might well have destroyed the tumor in its original site. The tumor might even have arisen from islands of squamous epithelium which are known to remain on occasion intact within the erosion area.

The author has never seen a squamous cell carcinoma of the cervix which did not arise from the surface epithelium. Transitions from benign epidermization to carcinoma are unknown. In order to prove that the newly formed epithelium of the epidermization may

be transformed into carcinoma it would be necessary to show that the latter arises not on the surface but deep in an epidermized gland. This has not yet been demonstrated. It obviously cannot be a common occurrence since with attention focused upon this question for several decades study of thousands of cases has failed to reveal it.

Similar proof must be demanded to demonstrate the so-called metaplasia of mucous epithelium into squamous epithelial carcinoma. Carcinoma must be shown to arise from areas where squamous epithelium and basal cell are absent. Multilayering of mucous cell carcinoma is not comparable and is readily differentiated from squamous cell carcinoma.



Fig 6 Same section as Fig 4.  $\times 275$



Fig 8 Same section as Fig 4.  $\times 110$



Fig 9, left Early carcinoma at the margin of glandular erosion of the portio Low power

Fig 10 A part of Figure 9 under higher power Membrana propria broken

particularly in the early stages. Much of the abuse of the term metaplasia will vanish on adequate study of the histogenesis of epidermization and carcinoma.

Polyps, in spite of being covered by ripe squamous epithelium and exposed to irritation, do not become carcinomatous. This is probably due to the fact that there is no older squamous epithelium surrounding the area of epidermization to serve, as in the cervix, for the tissue of origin of the carcinoma. It is true that the squamous epithelium of an old epidermization has the same properties as the original squamous epithelium and might, under certain circumstances, age and give rise to carcinoma. This does not affect the general statement that carcinoma does not arise from active epidermization undergoing proliferation as in erosion healing.

One might conclude, then, that carcinoma and epidermization of erosion are two distinct and unrelated conditions. They both arise from the basal cells of the squamous epithelium at the margin of erosions. But epidermization is a benign restoration and, when completed, approximates the normal. Carcinoma does not arise directly from it.

#### DIAGNOSIS OF EARLY CARCINOMA IN ASSOCIATION WITH EROSION

The morphological distinctions between epidermization and early carcinoma have been considered in the first part of this paper. Both may spread over the surface and enter glands. For differential diagnostic purposes it is only necessary to keep the characteristics of each condition clearly in mind. The finer cellular histology is not useful at first and, under any circumstances, the usual fixation makes



Fig 11

Fig 12

Fig 13

Fig 11 Early carcinoma at the margin of a glandular erosion of the portio Low power

Fig 12 Another instance of early carcinoma at the

margin of a glandular erosion of the portio Low power

Fig 13 Early carcinoma on an ulceration of the portio Low power



Fig. 4 left Oblq brleln bte e lycarc om ndn rml pthl mat th surf fth  
 pot X 15

Fig. 5 B de h bte n alycarc m ndn rml pthl m th surf fth potio X 4

demonstration of these features difficult or impossible. The morphological changes which represent the very beginning of malignancy are not known. Mitoses are not usually found in early stages. Abnormal mitotic figures present in later stages are not found in beginning carcinoma. Most of the mitotic deviations described in the literature are evidences of cellular regression. Regression is not characteristic of very early carcinoma with the occasional exception of that caused by severe inflammation.

It is characteristic of benign epidermization that having filled the glands its demands are satisfied. Even the original shape of the glands is still recognizable. Later when the epithelium ripens the glands may become dilated. The proliferation however is stopped

by pressure. The benign epithelium can invade only along these glands. In contrast distinction the carcinoma uses the glands only as a matter of convenience. It continues its proliferative course extending and deforming the glands and ultimately breaking through the basal membrane directly to invade the underlying tissue. Direct invasion of the connective tissue may occur in early stages of carcinoma particularly at the surface as will be described later. Benign epidermization does not extend beyond the basal membrane.

Figure 9 shows a small carcinoma arising from the basal cell of the normal squamous epithelium at the margin of an erosion. It has invaded and partially filled 3 glands. A small outgrowth of tumor may be seen extending into the connective tissue from the middle gland. This is seen under higher magnification near the left side in Figure 10. A strip of basal cell is forcing its way through the gland basement membrane. The lumen of the gland is not completely filled. The invasion through the basement membrane and into the connective tissue proves of course that this is a carcinoma. This fact can be readily recognized as well from the abnormal cell form.

In Figure 11 an early carcinoma may be seen pushing its way into gland not only beneath the columnar epithelium but in large solid masses which are virtually melting away the original epithelium. Again the carcinoma arises from the normal squamous epithelium at the margin of a glandular erosion and invades the glands nearest to it. This is repeatedly observed and Figure 12 shows another such case. Not all carcinomas begin here. If there are no glands in the erosion or ulcer the early carcinoma may directly invade



Fig. 6 Th b l f q m us pthl m  
 pl ed by c m Th c ma is l ad g  
 the p b l w fth rml pthl m X 5

Fig. 17, left. Early carcinoma at the surface in the cervical canal.  $\times 10$ .Fig. 18. Superficial carcinoma of the cervical canal.  $\times 140$ .

the underlying connective tissue. This is apparently accomplished with particular ease when the surface is made up of granulation tissue (Fig. 15). This section also clearly demonstrates the origin of the carcinoma from the basal cells of the normal squamous epithelium. That the epithelium is not destroyed proves that the carcinoma is young.

The early squamous cell carcinoma is usually composed of unripe or middle ripe cells although there are exceptions to this. The carcinoma appears riper at the surface than in the deeper areas. This is due not only to the fact that the deeper portions are younger but also to the effects of exposure of the upper portions to surface conditions.

Carcinoma arising from the epithelium at the margins of an erosion may spread not only over the erosion but away from it, thus de-

stroying the normal epithelium and invading beneath it. This action often proceeds in a typical manner, pushing forward obliquely under the normal squamous epithelium as shown in Figure 14. In this biopsy specimen excised from the portio, the carcinoma is readily recognized on the right. The remnants of the normal squamous epithelium may be seen on the surface while the deeper layers are being destroyed and replaced by the carcinoma.

The basal cell layers of the carcinoma show the greatest rapidity of growth. They first extend laterally, destroying the deeper layer of the normal epithelium. The carcinoma then becomes multilayered by virtue of horizontal cell division and proceeds to destroy the more superficial parts of the normal epithelium. The result is an oblique junction of

Fig. 19, left. Very early carcinoma of the cervical canal.  $\times 252$ .Fig. 20. Same case as Figure 19, 3 months later.  $\times 210$ .



## SURGERY GYNECOLOGY AND OBSTETRICS

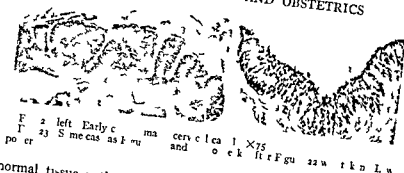


Fig. 2 left Early carcinoma cervix and o. c. k. Fig. 23 w. t. k. L. w. po. er. S. m. e. c. a. s. k. r. u. and o. c. k. Fig. 23 w. t. k. L. w.

tumor and normal tissue with an angle of about 45 degrees. The activity of the carcinoma cells is only one factor in the production of this angular junction. Variations in resistance to growth may play a part. The more dense the cornified upper layers and the less dense the lower layers as in the presence of round cell infiltration the greater the tendency to angulation of the line at which tumor and normal tissue meet. The consistency of the connective tissue is also of importance. Figure 13 shows a very small angle between normal epithelium and tumor advancing from right to left. Figures 14 and 15 are taken from the same superficial carcinoma. While the basal membrane in Figure 15 seems to be resistant it has already been broken through in the area represented by Figure 14. Figure 16 is taken from the base of a glandular cervical polyp. The patient was 62 years old and showed a carcinoma which had already destroyed a part of the cervical connective tissue and extended over the surface of the polyp. The squamous epithelium covering the polyp has not changed to carcinoma.

The latter has extended beneath the benign epithelium and has destroyed the normal basal layers. The borderline between the tumor cells and the remainder of the overlying normal epithelium is not sharp. The carcinoma cells are irregularly shaped with large darkly stained nuclei. They have invaded the remainder of the benign epithelium toward the surface. About half way between basal membrane and surface may be seen several remnants of dead cells. These are not secretion vacuoles but represent the debris remaining after cellular dissolution. The basal membrane is also undergoing dissolution. The fact that normal epithelium covers the carcinoma is only evidence of speedy horizontal extension of the carcinoma at the basal level.

## CERVICAL CARCINOMA FOUND IN CURETTAGE MATERIAL

Since the first occasion on which minute pieces of carcinomatous tissue belong to

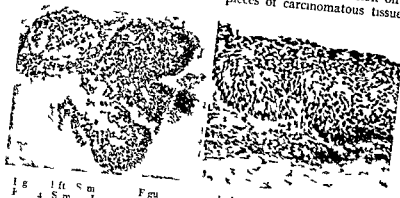


Fig. 13 left S. m. e. c. a. s. k. r. u. Fig. 14 S. m. e. c. a. s. k. r. u.

the cervix, were found in curettage material, it has been a routine procedure to cut the blocks of every curettage at multiple levels. As a result of this, a considerable group of very early squamous cell carcinomas were discovered. Garlach, in the author's laboratory, was able to collect a considerable number of these. Descriptions of them will be published in detail in the near future as part of 80 early carcinomas which have been collected over a 3 year period. There is every reason to believe that this is an observation which is of significant importance.

Most of these findings were the result of unintentional curettage of the cervical canal. They were found as small masses and strips of atypical, unripe, multilayered epithelium scattered among the pieces of endometrium. The diagnosis in most cases presented no difficulty.

Most often the carcinoma cells are found in flat strips 5 to 10 millimeters in length. Figure 17, however, shows a section through a small papilla about 5 to 6 millimeters in diameter. There is a delicate stroma with dilated capillaries and lymphocytic infiltration. This stroma seems to be newly formed and it may represent the beginning of a papillomatous form of carcinoma. The patient was 36 years old and had had her last normal menstrual period 3 months before. She had noted vaginal bleeding for only 14 days. The endometrium was in normal secretion phase. The uterus, removed 16 days after curettage, contained a small superficial carcinoma in the cervix. The vaginal surface of the portio was free of carcinoma. The early bleeding may well have been due to the exophytic growth of the tumor.

Figure 18 is from a specimen obtained in a 49 year old woman with hyperplasia of the endometrium. The illustrated small piece of squamous cell carcinoma was found in the curettage material. This combination of endometrial hyperplasia and cervical carcinoma is a rare occurrence. The removed uterus showed a myoma in the fundus. The carcinoma was found in the cervical canal but had remained superficial, perhaps as a result of the exceptionally strong membrana propria.

The 2 following cases present interesting problems since repeated curettages were carried out. The first was a 41 year old woman in whom curettage was done because of irregular bleeding. The endometrium showed nothing of importance. A few small pieces of cervical mucosa (Fig. 19) showed suspicious epithelium. Instead of the normal layering of the epithelium with a single basal cell layer, the epithelium here has a tendency to be similar at all levels. The basal cells do not show the normal clear definition. The nuclei are close together, rich in chromatin, and somewhat irregular in position, shape, and size. It is still more important to note that the cells in the levels above this show similarity to basal cells. They have large nuclei of irregular form, but for the most part they are elongated and have a radial arrangement. They contain less chromatin than the basal row but much more than normal squamous epithelium. The basal membrane is indistinct and invaded by lymphocytes which have infiltrated the underlying connective tissue.

Because the epithelium appeared very suspicious, the cervix was curetted 3 months later and the slightly eroded area on the portio excised. The material is shown in Figure 20. The multilayered epithelial cells have a greater irregularity of form than before and are packed tightly together in an irregular manner. The basal cell layer is absent. The nuclei at all levels are richer in chromatin, and the demarcation between the squamous epithelium and the connective tissue is not as clear as before. The lymphocytic infiltration is not striking. The epithelium has not invaded the connective tissue but is seen elsewhere to have begun to invade the mouth of a gland, melting down the mucous epithelium in the process. The uterus, removed some days later, showed the same epithelium invading the connective tissue in a few areas.

In the second case, curettage was done for irregular bleeding, and a small piece of fairly superficial squamous epithelial cell carcinoma was found. Although the basal membrane seems to be well preserved, there are quite atypical projections (Fig. 21). The epithelial cells of these appear more unripe than

# THE LIMITATIONS OF THE ROENTGEN DIAGNOSIS OF FRACTURES

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**S**INCE the advent of x rays the list of time honored classical signs of fractures has been increased by one which is at least of equal value. In recent years many courts in this country and abroad have pronounced physicians negligent who failed to use the x ray in the diagnosis of suspected fractures and have thus marked the radiological approach as superior to all other diagnostic procedures. The erroneous conception has developed that an x ray report is something objective and indisputable not open to human fallacies and personal factors of training and knowledge. The fact that the roentgenogram does not lie is that it represents objective physical conditions does not imply that the one who reads it necessarily interprets these physical conditions correctly.

This makes it incumbent on all who utilize the x ray in the diagnosis of fractures to familiarize themselves with the limitations of roentgenological approach. It is the purpose of this paper to discuss these limitations in connection with the principal points of evidence obtained from the roentgenogram. Considering it the function of radiological procedure (1) to demonstrate the presence or absence of bone fracture (2) to depict the normal or pathological character of the fractured bone (3) to disclose the displacement of fragments and (4) to show the course and progress of healing then this paper attempts to discuss the limitations of each of these points of x ray evidence.

## A ERROR OF NEGATIVE ROENTGEN DIAGNOSIS IN PRESENCE OF FRACTURE

*Prerequisites for x ray visibility of fracture*  
For the sake of this discussion it is assumed that x rays in each case are used properly under optimal conditions of radiographic

technique. Otherwise the field of evidence would be much more restricted. But sometimes due to the state of the patient it is neither feasible nor practicable to obtain the proper roentgenograms. Often the decision of the roentgenologist as to the choice of his procedure will represent a compromise between the demand for optimal visualization of the fracture and the caution required in handling a recently injured patient.

It is easy to realize that a fracture may not be apparent on roentgenograms if due to the condition of the patient the customary projections in two vertical planes cannot be utilized. But more relevant to the present discussion is the question are there fractures which do not show up on the roentgenogram even if all routine views have been employed? In this connection it is of course necessary to define the meaning of the term routine or standard views. The technique of x ray positioning is not static or fixed it develops with the advancement of roentgenological science of which it is a part and with the technical progress of radiographic apparatus. But the following prerequisites for visibility of a fracture should be realized: (1) The dehiscence should at least be of macroscopic dimensions. (2) The x rays should traverse the bone approximately in the direction of the fracture gap. (3) The fracture should not be obscured by dense radiopaque bone. (4) In case there is no cleavage at the fracture site displacement of the fragments should have produced distinct structural or contour changes. If any one of these conditions is not fulfilled the fracture will most often be invisible. Further technical factors usually necessary for the demonstration of fractures are: (5) that the fracture line be brought as close to the film as possible (6) that the exposure be adjusted to the part in question and (7) that in locations where combined fractures are frequent all parts be roentgenographed which are potential

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sites of additional bone injuries. Examples based on our own experience or chosen from the literature will illustrate and amplify these statements.

*Nonvisualization due to location of fracture in cartilage.* Since a fracture is customarily defined as a break in bone or cartilage, it is necessary to point out that cartilaginous fracture cannot be diagnosed from the roentgenogram. This includes fractures extending into the joint cartilage, fractures of the menisci and cartilaginous parts of ribs, and traumatic separations of epiphyses so long as these are not ossified.

*Nonvisualization due to minute size of fracture gap.* As has been pointed out, the fracture gap must be at least of macroscopic dimensions in order to be visible on the x-ray film. Fissures through the labyrinth of the inner ear may be so fine that they can be demonstrated only microscopically. Then the roentgenogram is of course negative. In metacarpals, metatarsals, and navicular of the hand there occur cracks so minute in width that they cannot be revealed in any projection. In these cases a second roentgenogram after 1 to 3 weeks may demonstrate the fissure after absorption of the damaged trabeculae has led to widening of the gap.

As in the examples just named the microscopic size of the destruction may also be the cause for negative findings in the early stage of Kuemmel's disease of the spinal column. Later, when the damaged trabeculae have been removed, the vertebral body, deprived of the necessary support, collapses (Brailsford). According to this interpretation Kuemmel's disease would be a compression fracture with the fresh injury beyond range of x-ray demonstrability.

The volar-dorsal view, or oblique projections, may depict fractures of the metacarpals and metatarsals otherwise not visible. It seems that insufficient understanding of the limitations of roentgenological procedure is partly responsible for the controversial discussion on the etiology and pathology of "March foot" or "Deutschlaender's disease." With Schunz and Schnek we assume that we are dealing here with invisible fissures of the metatarsals, especially of the second.

Other regions where minute cracks may escape roentgen diagnosis are the tibial condyles and shaft, the patella, the capitulum of the radius. The meshwork of longitudinal tracts of trabeculae in these areas is coarse and wide enough to conceal fine fissures.

*Nonvisualization due to insufficient number or wrong choice of projections.* One of the essential factors in determining the visibility of fractures is the direction of the x-rays in relation to the fracture line. The dehiscence will be depicted only if the x-rays traverse the bone in the direction of the gap. In most cases the customary projections in two planes vertical to each other will be sufficient to demonstrate the fracture line. Practical experience, as well as consideration of the fundamental laws of projective geometry, prove that one projection is not sufficient to establish presence or absence of a fracture. While it is easy to utilize this knowledge for most of the long bones, in some regions a second projection requires modern technical facilities and skill, often also a certain ability for improvisation. Areas belonging to this group are the shoulder where a second projection has to be insisted upon in case of questionable fracture of the humeral head and neck and of scapula and clavicle.

But in numerous locations even two views may not be sufficient to demonstrate a supposed fracture. Complex or unfavorably located bones or parts of bones, like the sternum, angle of ribs, skull, spinal column including the sacrum, coronoid process of ulna, navicular of hand, os pubis, condylar end of femur, patella, malleolar region of ankle, talus, calcaneus, these often require more than the time-honored two projections. Here the number of fractures overlooked will decrease in direct proportion to the number of projections employed. The underlying principle of these additional projections is usually an axial view, as in the case of the base of the skull, the os pubis, patella, talus and calcaneus, or oblique views as in case of sternum, ribs, spinal column including the sacrum, ankle, navicular of the hand, metacarpals, and metatarsals. In case of ankylosed joints, skull cap, ribs, chip fractures at articular parts of phalanges, atypical positions can often be used to great

advantage. Thus while unintentional deviation from standard positions by careless x ray technicians may obscure many fractures, indiscriminate use of nonroutine views by the resourceful roentgenologist will help to reveal fractures which cannot be discerned otherwise. Stereoscopic views in one projection are often not satisfactory for replacing projections from different angles. Of interest is a statistical study which was made by Hunsberger. He demonstrates that in a series of 103 fractures in which three or more views were used 36 or 35 per cent showed up in only a single view.

*Non-routine use of skull fracture.* The most complex parts of the skeleton of course offer the greatest difficulties in revealing the fracture line. Thus it is not surprising that in skull and spinal column we encounter the greatest number of negative x ray findings in presence of fracture. In many cases of fresh head injuries it is not in the interest of the patient to take recourse to radiographic procedure at all. In other cases the radiologist will have to be satisfied with few standard views in frontal and sagittal planes, preferably stereoscopic and desist from special views such as might be required by the location of the injury. Under these circumstances one should not be surprised to miss a large number of clinically certain fractures. Linear fractures of the base of the skull produce the greatest diagnostic difficulties. Since they can usually be demonstrated only if the x rays traverse the bone in the direction of the fracture line, it is more or less a matter of chance whether these fractures are depicted or not. Special projections as in the case of the petrous bone improve of course the prospects of revealing the dehiscence. Isolated linear fractures of the roof of the orbit and the wall of the pneumatic spaces may also not be revealed on the roentgenogram. In the latter case the opacity of the sinus as produced by hemorrhage may give a clue. Fractures of the face and jaw very often require the use of half axial and oblique positions.

*Non-routine use of vertebral fracture.* Fractures of the spinal column are in most cases compression fractures and are therefore characterized roentgenologically by the absence of

a fracture dehiscence. That introduces a new element in the x ray diagnosis of the injury, making it incumbent on the roentgenologist to look for contour or structural changes which are due to displacement of the fragments. Here again the roentgenologist will have to increase the number of so called standard views in order to make full use of the possibilities of x ray procedure. The time honored anteroposterior view even stereoscopically is certainly not sufficient. Modern technique requires 5 to 7 feet focus film distance to avoid distortion in the off center portions of the film. According to Jordan a complete roentgen analysis of the spine in case of fracture consists of the following exposures: (1) anteroposterior and lateral long distance views of the lumbodorsal spine with the patient standing or sitting; (2) anteroposterior and lateral long distance views of the cervical spine with the patient sitting; (3) anteroposterior cone film of the lumbosacral and sacroiliac region; (4) right and left oblique views of the lumbosacral spine showing the intervertebral joints; (5) right and left oblique views of the dorsal spine showing the intervertebral joints in this region. As expensive and time consuming as this approach may be, it represents the only scientifically correct answer to the problem of roentgen demonstration of spinal injuries. Unfortunately external circumstances and clinical factors may often not permit this extensive procedure. Since the clinical symptom of pain is a very inconclusive means of localizing the area involved, it is wise to include the entire spine in the range of our examination. The best obtainable bone detail is required to reveal minute compression fractures which are characterized by a slight condensation of the spongy texture and minor annulation of the individual vertical axes of the vertebral bodies.

Spot films taken with small cone or rotating anode tube films are indispensable in these cases. Optimal photographic technique together with appropriate oblique views are necessary for demonstration of injuries to the pedicles, the laminae and the articular processes. Although not rare, they are not often disclosed in routine anteroposterior or lateral views.

*Difficulty of fracture diagnosis in the absence of a fracture gap* Fractures of the vertebral bodies are not the only group of bone injuries characterized by absence of a fracture gap. Calcaneus talus, lunate, navicular, head and neck of femur and humerus, distal end of radius are other regions where fractures are often revealed only by changes in contour and structure of the bone due to displacement or impaction of fragments. It therefore requires films of optimal quality to disclose the finer textural details.

*Difficulty of fracture diagnosis due to superimposition* In some regions the fracture gap, although present, may not be apparent, due to superimposition of other portions of the same bone or of other bones. Fractures of the femoral neck illustrate this well. In external rotation of the leg the femoral neck is foreshortened and obscured by the shadow of the greater trochanter. Thus impacted fractures of the neck may not be diagnosed at all, if the patient is roentgenographed in the position of external rotation, which the fractured leg naturally assumes. Fractures of the vertebral arch may not be visible on anteroposterior view, as they are obscured by the vertebral body. In skull fractures the fracture line is frequently not shown due to superimposition of other portions of the skull. In lateral views of the forearm and leg, parts of the bones which are frequently the site of fracture are projected into the other bone. Thus the head of the radius is obscured partly by the coronoid process of the ulna, and the distal end of the fibula is superimposed over the posterior distal edge of the tibia. If these areas are not carefully checked in other projections, including oblique views, the fracture may be completely overlooked or may be attributed to the wrong bone.

*Difficulty of fracture diagnosis due to technical factors* In addition to the principal factors exemplified which decide the visibility of a fracture, other requirements also here listed are closeness of the fractured area to the film and proper exposure. The first may be illustrated by the difficulty encountered in obtaining a clear film of a fractured elbow or knee joint locked in the position of flexion. Here the details of the fracture may not be visual-

ized unless the film is brought close to the flexed joint, either by the use of a curved film or by taking two views in the anteroposterior direction, one for the humeral part of the joint and the other for the radioulnar part (Hunsberger). The same remarks apply to the knee joint.

The importance of adjusting the exposure to the part in question is exemplified by the fact that fractures of the spinous processes of the vertebral column will be overlooked on lateral view, if the exposure is directed toward demonstration of the bodies of the vertebrae.

*Nonvisualization in case of multiple fracture* Many fractures are not revealed because the injured part is not included in the x-ray examination. This is especially the case in multiple fractures. The radiologist and clinician are satisfied if one fracture is demonstrated and neglect to study other portions of the skeleton. Thus a fracture of the navicular is not diagnosed in case of accompanying fracture of the radius, a calcaneal fracture is not discerned if combined with a malleolar fracture. A characteristic injury in which one fracture is frequently overlooked is a spiral fracture in the middle or lower third of the tibial shaft combined with a fracture of the fibula below the head. The clinical symptoms of pain and tenderness are often not conclusive means of locating multiple fractures, as is proved in the spinal column. Here isolated fractures may occur at different levels with uninjured vertebrae between them. Frequently pain is referred to the lumbosacral region, when the fracture is actually located in the dorsal vertebrae. Some fractures often occur on both sides of the body, e.g., fractures of calcaneus and radius.

#### B ERROR OF POSITIVE ROENTGEN DIAGNOSIS OF FRACTURE IN THE ABSENCE OF FRACTURE

Our discussion so far has shown that in certain regions the chances of overlooking the presence of a fracture are very real. Yet there is even a greater and psychologically more understandable chance of diagnosing a fracture where none is present, an error based on false interpretation of normal or pathological conditions which closely imitate the x-ray appearance of bone injuries. A great number

of these mistakes could be avoided by a thorough knowledge of x ray anatomy comprising not only the x ray appearance of normal structures at various ages but also the numerous variations of the skeleton which are especially apt to be mistaken for traumatic changes. Other misinterpretations are almost unavoidable at the time of the first diagnosis; they can be cleared up only in due course of time by further clinical and x ray check ups. There remains a final group of cases the diagnostic difficulties of which cannot be solved at all with the present state of our knowledge. They touch upon problems which are under scientific investigation or have received conflicting answers in the literature. Although these problems are academic in scope and approach they are frequently of great practical importance in individual cases when the decision has to be made whether a certain condition is traumatic or developmental in origin. The later discussion on the bipartite navicular on pondylosithesis and the Looser zone of transformation will illustrate this.

It will be recalled that for the scope of the present paper it is assumed that the x rays are utilized under optimal conditions of exposure and positioning including in many cases a necessary and very helpful comparison with the opposite side. In investigating the sources of diagnostic errors of interpretation it is not intended to enumerate all possible pitfalls of radiological fracture diagnosis. This discussion attempts only to state and demonstrate on illustrative material the principal sources of errors in the roentgen interpretation of fractures to point out those which are unavoidable and to show means of avoiding the others.

### 1. Normal Structures Imitating Fracture

Since the most characteristic radiological signs of a fracture are the fracture line or in absence of a gap the structural and contour changes concomitant with the displacement of the fragments anything simulating a fracture line or the alterations in structure and contour of the bone as produced by a fracture may be mistaken for a fracture. In general any anatomical excitation which leads to interruption of the expected continuity of bone

can and has been misinterpreted as a fracture.

*Soft structures.* Thus as far as soft structures are concerned gas bubbles in intestines superimposed over the spinal column or the pelvic folds of skin and underlying tissue e.g. in the region of the axilla buttocks toes or the edges of muscles such as the lateral border of the psoas may produce an apparent discontinuity in the bone over which they are projected but they can be identified if one follows the questionable line beyond the shadow of the bone.

*Epiphyseal lines.* Sufficient command of x ray anatomy will prevent misinterpretation of the epiphyseal lines as fractures. A further safeguard against this common error is a knowledge of the distinguishing features between epiphyseal and fracture lines. The epiphyseal line is usually of even width throughout the fracture line is often wider on one end than on the other the contours of an epiphyseal line are usually smooth and regular the edges rounded the contours of a fracture line are rugged and irregular the edges sharp (Ferguson and Clapham and Swaberg). Yet some young epiphyseal lines are fairly irregular as e.g. the of the acromioclavicular joint of humerus olecranon tuberculum but the other characteristics just named still hold true. Often a comparison with the opposite side will show identical fin lines there will clear up the question.

The differential diagnostic difficulties are greater when we deal with an old injury where nonunion of the fragments is suspected. Here as in epiphyseal lines the contours may be smooth the edges rounded but the presence of some reparative signs as sclerosis and callus formation in case of fracture may still afford a possibility of diagnosis (Ferguson).

Due to general endocrine disturbance or some unknown local cause epiphyseal lines may persist throughout life. If they persist they are not suspected and if their general characteristics are disregarded they are easily mistaken for fracture. A typical example is the acromioclavicular joint which occurs at the same place where a fracture might be located.

*Varia nts and anomalies of the skeleton.* There is a large group of variations of the skeleton commonly classified under the head

ing of "accessory bones," that may deceive the beginner and often also mislead the experienced. These supernumerary bones arise from separate centers of ossification representing persistence of "embryonic vestiges which usually disappear" (McGregor). Other accessory bones are due to an abnormal division of usually solitary ossification centers or to failure of centers of ossification to unite. Any one of these abnormal bones may be falsely regarded as of traumatic origin, or at least give rise to diagnostic difficulties. Again in order to avoid these errors their possible sites should be familiar to anyone who interprets x-ray films of bones. Study of their contours and of the outline of the adjacent bones as well as comparison with the opposite side will in most cases clear up their derivation. In recent accident cases control examinations in time intervals will demonstrate traumatic etiology by appearance of reparative signs. But old injuries with pseudarthrosis of the fragments can sometimes not be differentiated from congenital nonunion. In the hand and foot the origin of supernumerary ossicles is frequently an object of heated discussion in medicolegal cases.

*Variations in the bones of the hand and foot* A typical example is the divided navicular, which Watkins has called the most troublesome anomaly in the hand. Especially puzzling are cases with recent traumatic history in which the smooth, dense contours of the two fragments forming the bipartite navicular preclude the possibility of recent traumatic origin of the division. Here the differential diagnosis between congenital bipartition and old traumatic nonunion has to be made. Detailed study of the fragment outlines usually does not help, since the contours in old injuries will also be smooth and well defined. There is usually no displacement in either case. The problem of the divided navicular of the hand is typical of the difficulties which may also arise in other regions. The foot is a favored location of supernumerary bones which may occur at the same site as fractures. Their frequency varies from 10 to 12 per cent for the tibiale externum and os trigonum to less than 1 per cent for others. They may be bilateral or unilateral. To com-

plicate the problem still more, supernumerary bones may actually fracture, but may also consist of several bony nuclei as the result of multiple anlage. A good example of this is the bipartite medial sesamoid bone in the first metatarsophalangeal joint. Clinically verified fracture of the same sesamoid has also been described. The characteristics of contour and texture of fractures as compared with the outline and structure of accessory bones should be made use of in the differential diagnosis. Accessory bones may show great variation in size. If they are faint and small, differentiation from chip fracture becomes a difficult problem. According to Ferguson a small bone mass should not be pronounced a fracture fragment unless a corresponding defect has been demonstrated in the bone from which the fragment is supposedly derived.

*Variations in the bones of the trunk* In the spinal column there are a number of variations whose differentiation from fractures may cause considerable difficulties. An example of an avoidable yet common error in diagnosis is to mistake the independence of the costal element of the first lumbar vertebra for traumatic separation. The transverse process of the first lumbar vertebra hardly ever shows an isolated fracture. In contrast to this variation the differentiation of an accessory center of the articular process of a vertebra from fracture of the same process is not so easy. Usually the inferior articular processes of the lumbar spine are affected, and the accessory center is separated from the process by a translucent transverse line.

The vertebral abnormality which has probably produced the widest and most controversial discussion is spondylolisthesis. One school considers it a congenital defect of continuity in the interarticular portion of the vertebral arch, based on nonunion of centers of ossification of the fourth or fifth lumbar vertebra. Others have explained the condition as due to an early trauma in the fetus, during parturition, or in infancy. A third group regards spondylolisthesis as acquired in life and produced not by an acute trauma, but by chronic mild injuries or the stress and strain of abnormal weight distribution on a less



resistant area. On the other hand true fracture of the same region might also occur. Meticulous technique and lateral and oblique views are necessary to establish the details which might afford a possibility of differential diagnosis. The final decision between true fracture and congenital malformation often must be left in suspense by the radiologist.

*Sutures and vascular grooves.* Developmental features in the skull which are likely to be mistaken for fractures are suture lines. On sagittal views the sutures between the temporal squama and adjacent bones are often misinterpreted as fractures. Difficult to identify are atypical suture lines which occur within the frontal or parietal bone and the occiput. These sutures may persist throughout life and imitate fractures. In general the following points should be observed (Goldhamer and Swanberg): the sutures do not extend over more than one bone, while fracture lines may cross over two neighboring bones; fracture lines are usually straight, sutures may be serrated; borders of sutures appear dense as compared with margins of fractures. Traumatic diastasis of sutures is often questionable since the apparent width of a suture on the roentgenogram depends also on the distance of the suture from the film.

Even more deceiving than suture lines are the vascular markings of the skull. The middle meningeal artery and its branches are the most important of the vessels producing grooves on the inner table of the skull. They are represented on the roentgenogram by transparent lines. Their typical location, their course, their width and lesser degree of transparency may help to differentiate them from fractures. But sometimes especially if a fissure follows the course of an artery the diagnosis will be difficult. Not only in the skull have vascular markings been mistaken for fractures. Nutritional vessels in vertebrae, scapula, humerus, radius, ulna, metacarpals and phalanges and ilium are on record as having been confused with fractures.

## 2. Pathological Conditions of the Skeleton Simulating Fracture

So far in this section of the paper we have discussed normal appearances of the skeleton

and congenital variations of the normal simulating the roentgen signs of fracture. But there is a wide range of pathological conditions the x-ray signs of which can and have been falsely interpreted as fractures. Spondyloolisthesis which represents a borderline subject has already been discussed.

*Para articular ossifications.* Early x-ray examination will clear up the nature of questionable posttraumatic para articular ossifications in the neighborhood of the medial condyle of the femur, the greater tubercle of the humerus, the medial epicondyle of the humerus, the lunate. The absence of such shadows on x-ray films immediately after injuries and their later appearance rules out fracture detachments and leaves the alternative diagnoses of heterotopic bone formation developed from small pieces of periosteum freed by trauma or metaplastic calcification and subsequent ossification of young connective tissue (Crilovich). The diagnostic difficulties are much greater if no early x-ray film exists; then also traumatic detachment of a scale-like fragment of bone has to be considered. Such detachments are especially common on the greater tubercle of the humerus. Here a fourth possibility as the cause of these shadows comes into play, i.e. deposits of calcium in the subacromial and subdeltoid bursae and the tendinous insertions on a nontraumatic and constitutional basis, a disease known as periarthritis humeroscapularis.

Careful attention to Ferguson's rule that in case of traumatic detachment of bone the roentgenologist should look for a defect from which the fragment is derived together with scrupulous and variable technique adjusted to each individual case will help in the differentiation of many of these shadows. But there will remain a number of cases especially old injuries in which final identification of these questionable para articular structures from the roentgenogram is impossible.

Arthritic spurs on calcaneus, olecranon, intercondylar eminences of the knee joint and vertebral bodies may appear separated from adjacent bones and therefore simulate chip fracture while in reality they are connected by fibrous tissue which is not visible on the film.

**Aseptic necroses** Aseptic subchondral necrosis may produce pictures which closely simulate traumatic separations. While duplication of the bony center for the epiphysis of the tuberositas tibiae is normal, disorganization, fragmentation and necrosis, usually as a result of trauma, represents the condition known as Osgood-Schlatter's disease. It should be differentiated from true avulsion fractures which also occur in this area (Skinner, Ferguson). Similarly Kienboeck's disease of the lunate, osteochondritis of the knee, osteochondritis of the tarsal navicular and fragmentation and necrosis of the capitulum humeri in the elbow joint should not be confused with fracture. Strictly speaking it is a pathological fracture which we encounter in these cases, if we define as pathological fractures breaks in the continuity of bone as the result of some disease of the bone. Thus this problem would be part of the general task of the physician dealing with bone pathology to differentiate between traumatic and pathological interruption of bone continuity. Is it possible in all cases to identify a pathological fracture as such? In other words, will the signs of the accompanying pathological condition which produced the fracture always be demonstrable? As far as the epiphyseal necroses mentioned are concerned the following signs of the underlying pathology will usually facilitate a correct diagnosis: abnormal density, irregularity and disintegration of the fragments, which render impossible a reconstruction of the original shape of the bone from the elements present, often combined with cyst-like bone absorption in the neighborhood.

**Pathological fracture mistaken for traumatic fracture** In certain regions of the body the underlying pathology may be obscured due to the compression type of fracture. Thus a spontaneous fracture of a vertebra in senile osteoporosis, which is one of the commonest causes of pathological fracture, may be pronounced traumatic in etiology, since the underlying bone atrophy is not recognized in the collapsed bone. The same holds true for metastatic malignancy of the spine. Case history and x-ray examination of other parts of the spine and of the rest of the skeleton will usually clear up the diagnosis. If a plaster

cast is applied to a fracture before an x-ray film is taken, the shadow of the plaster may obscure the accompanying pathology, e.g., a bone cyst as experienced in one of my cases.

Paget's disease of the skeleton and osteogenesis imperfecta may lead to spontaneous fracture without producing on the roentgenogram any evidence of structural changes besides the fracture. But the transverse direction of the fracture gap should suggest the presence of bone pathology (Ferguson). Translucent lines on the convexity of long bones in Paget's disease have found conflicting interpretation. While Schmorl concludes that they are actually fissure fractures of the cortex due to local injury in presence of bone pathology, Brailsford does not believe them to be fractures at all, but interprets them as so-called "Looser's Umbauzonen," i.e., zones of transformation or metaplasia. Looser has described these zones as characterized histologically by lamellar bone resorption and substitution by partly calcified fibrocartilage, fibrous transformation of bone marrow, and marginal periosteal activity. They occur in osteomalacia, late rickets, and osteitis fibrosa cystica, but have also been reported as a disease *sui generis*. Continental authors have found them in the shaft of the tibia, fibula, neck of femur, in the pelvis and calcaneus, especially in young soldiers where there was no acute trauma. Here they are supposed to be due to chronic overloading, "wear and tear fractures" (Reischauer). Roberts and Vogt call them pseudofractures and have encountered them in the upper third of the tibial shaft in children in the absence of acute trauma. The latter authors concede that the exact nature of the disease is not known. Reischauer suggests that march fracture of the metatarsals and spondylolisthesis, also separation of part of the spinous process of the lowest cervical and first thoracic vertebrae as seen in ditch diggers, belong to this group. All in all the pathogenesis and classification of this interesting and complex condition are obscure.

#### C LIMITATIONS OF X-RAY PROCEDURE IN EVALUATION OF POSITION OF FRAGMENTS

So far it has been the purpose of this paper to demonstrate the limitations of the x-ray

diagnosis of fractures pointing out the difficulties and pitfalls of roentgenological evidence. It is likewise necessary however to recognize the further limitations of radiographic procedure in regard to information furnished on the position and displacement of fragments.

What has been said in reference to the diagnosis of fractures about the necessity of different projections in each case holds even more forcefully in eliciting detailed information on displacement. The literature of recent years gives full account of the need of views from different angles for evaluation of displacement in fractures of the femoral neck, shoulder, patella, talus, calcaneus, spinal column and others. Stereoscopic views are insufficient to replace additional projections.

In regard to fractures of the femoral neck one can justly say that introduction of the lateral projection has decisively influenced the treatment and prognosis of these injuries. Only complete visualization of the displacement before and during reduction and careful roentgenological check up after reduction will assure success in this treatment. Authorities have stated that omission of the lateral view is probably the most common cause of failure in reduction and nonunion.

The laws of projective geometry make us realize that angulation of fracture fragments toward or away from the plane of the x ray film leads to wrong evaluation of displacement. Lateral shift of the fragments will be pictured on the x ray film without distortion only if the displacement has taken place parallel to the x ray film. The only displacement which can be measured without error on the roentgenogram is the longitudinal if the proper projection has been chosen (Schunz). Rotation of one fragment upon another is hardest to evaluate by radiographic method and is only approximately possible if the film includes the joints proximally and distally to the fracture (Schnek).

At sites where parts of a long bone form a conspicuous angle as between shaft and neck of femur, this angle must of course be taken into consideration in reduction of fractures. It is in locations where this angle does not deviate much from 180 degrees that it is often overlooked in correction of displacements. Thus in reduc-

tion of fractures of the lower end of the humerus the so called carrying angle between humerus and forearm which in extension is 10 to 15 degrees has to be restored. In the same region the anteriorly open angle between the lower articular end of the humerus and the shaft calls for attention. On the lateral roentgenogram of the wrist a plane laid through the joint surface of the lower end of the radius normally forms an angle with the axis of the radius which is less than 90 degrees. The angle is often considerably increased in compression fractures of the lower end of the radius (Skinner). If in correction of the displacement the angle is just reduced to 90 degrees it will result in considerable restriction of flexion. Similar important angles to be taken into consideration in the reduction of displacements are the angle between tibial shaft and proximal articular portion of the tibia, the calcaneal angle as well as the normal curvatures of femur, radius, ulna, metacarpals and spinal column. If this normal anatomical relationship of portions of bones is to be appreciated to its proper extent, simple inspection of displacements on roentgenograms is not sufficient. The axes of bones will have to be marked out in the roentgenogram and angles measured in order to obtain the best possible functional results.

Since parts of the fracture line may not be depicted on the x ray film a fracture may appear incomplete in cases in which it is actually a complete break. The more frequent application of the lateral view in fractures of the femoral neck has also proved that impactions do not occur as often as thought and that the impression of impaction is produced on the anteroposterior film by overlapping of the fragments.

#### D. LIMITATIONS OF X RAY EVIDENCE OF HEALING OF FRACTURE

One of the most important problems in connection with the roentgen symptomatology of fracture is the evidence furnished as to the healing of fractures and the progress and stability of bony union. The following are the x ray signs commonly used in the evaluation of posttraumatic bone reconstruction: (1) obliteration of the fracture line, (2) amount and

density of the visible callus, (3) formation of bony trabeculae bridging the fracture gap. Taken separately these signs are of questionable value. None of them affords absolute certainty of bone union, nor does their absence prove nonunion.

Thus a fracture line may become invisible, although present, as in case of pseudarthrosis. Exuberant callus is formed, obscuring the cleavage on the roentgenogram, or if, due to the direction of the x-rays, the fracture gap is not visualized. On the other hand clinical consolidation of a fracture may be present and yet the fracture line may still be visible, wholly, or in part.

Since the amount of callus formation depends on many factors which do not have any bearing on the final re-establishment of bony continuity, it is evident that the quantity of callus visible in the roentgenogram is no criterion for the firmness of bony union. The better the alignment the less callus is formed. Skinner points out that in some fractures without displacement no callus can be demonstrated and yet healing may be complete. On the other hand excessive and premature movements of the fragments may lead to exuberant callus and pseudarthrosis at the same time. The roentgenological density of callus depends of course on the amount of calcium present in the callus. But the mineral content of callus is not the only factor responsible for its firmness. This depends also, as Haebler and Reiss have shown, on the proportion of colloids and crystalloids in the callus and on the water content of the colloids. The latter two factors are of course not accessible to roentgen determination. This leads to the more elementary question: what part of the healing process of fractures is revealed by x-ray? Ham, Lisdall and Drake separated the two phases of bone repair: callus formation and calcification, by artificial means in animals whose bones had been fractured, and demonstrated that only the process of mineralization was disclosed by x-ray. Their experiments suggest the possibility that certain cases of apparent meager or retarded union or even nonunion are in reality cases of noncalcified callus. It now is evident why every case of healing fracture presents a roentgenologically latent period

of bone repair of from 10 days to 3 or more weeks and why the palpable callus is often more voluminous than the roentgenogram shows.

The third x-ray sign of re-establishment of bone continuity, i.e., formation of bone trabeculae across the fracture gap, may be deceiving since it may be simulated by a slight change in the angle under which the film is taken. In this case the bone texture in front of or behind the fracture gap may apparently be traced across the fracture gap, although in reality the fracture line has not been obliterated. Portable equipment is usually not satisfactory in eliciting the signs of bony union. It is especially in the femoral neck that the x-ray evidence of bony union has been unreliable. Skinner, and Garland and Hill warn against evaluation of films of fractures in plaster casts for evidence of healing. Even more difficult is the roentgenological evaluation of bone repair in fractures of the spinal column. Neither anteroposterior nor lateral views afford roentgenograms which show sufficient detail to depict the extent of the callus formation.

For correct appraisal of the final result of a fracture, it is necessary to differentiate sharply between delayed union and pseudarthrosis. The diagnosis of pseudarthrosis requires positive evidence expressed by the following x-ray signs: rounding-off or tapering and sclerosis of adjacent ends of bone fragments, visible diastasis between the fragments, retrogressive processes in the callus (Pfab).

Other signs sometimes used to verify bone repair are: maintenance of relative position of fragments after a trial of weight bearing, maintenance of relative position of fragments demonstrated on roentgenograms taken in different positions of the articulating parts (Lewis). But, as conceded by Garland and Hill, internal fixation by nail in fractures of the femoral neck may maintain the alignment of fragments and permit weight bearing without bony union having taken place.

Summarizing this discussion on the value of x-ray examinations for the appraisal of bony repair, it can be concluded that x-ray evidence of bony union has to be used with great reservation and only in conjunction with other clinical findings.

The problem of demonstration of the process of fracture repair on the roentgenogram is important also from the medicolegal point of view. In this connection the following questions may arise: Can the x ray signs of fracture disappear so completely that occurrence of a fracture in the past history of the patient cannot be established from the film? The answer is in the affirmative. Reconstruction of the bony pattern may be so perfect that no trace of the fracture is left in the roentgenogram. Also of medicolegal importance is the question arising in case the presence of an old fracture is disclosed on the film whether the approximate date of the injury can be established. *A priori* one would assume that the gradual disappearance of the fracture line and the consecutive reparative and retrogressive changes in the callus would afford some means of determining the time of fracture. In general it can be said that the younger the fracture i.e. the more active the evolutionary changes in bone repair the closer one will come in estimating the correct date of the fracture. Rentsch points out that up to one year after the injury it is possible to determine approximately the date of fracture from the film. But even here great variations occur depending on the location of the fracture, the displacement of the fragments, the age of the patient, the type of treatment, constitutional factors etc. After 1 year's duration it is almost impossible to arrive at the date of the fracture from study of the roentgenogram. Leaving aside fractures of the skull the roentgen picture of the average fracture will become stationary after that period so that no further changes might be expected.

#### CONCLUSIONS

In the light of the described limitations and in order to make full use of the diagnostic possibilities of the roentgen rays realization of the following facts is necessary:

1. The x ray examination has to be preceded and checked by detailed physical examination which in evaluation of fracture repair is equal or superior to x ray studies.
2. More complex skeletal structures require modern shockproof and powerful equipment and complete command of the technique

of positioning. The latter includes the utilization of oblique axial and long distance views and if necessary of atypical improvised projections. The best and most comprehensive technique is especially needed in evaluation of displacements.

3. For the physician dealing with traumatic bone surgery it is necessary to master the laws of x ray physics especially of projective geometry. Further requirements are a thorough knowledge of x ray anatomy comprising not only the x ray appearance of normal structures at various ages but also of the numerous variations of the skeleton. Knowledge of normal anatomical angles and determination of the normal anatomical relationship of portions of individual bones is part of the field of x ray anatomy. In order to distinguish between traumatic and pathological interruption of bone continuity one must also be familiar with the x ray symptomatology of bone diseases.

4. X ray examination immediately after a doubtful injury may remove otherwise unavoidable diagnostic difficulties and will put medicolegal testimony on more solid ground. It will be especially helpful in the differentiation between fractures and accessory bones and in the identification of posttraumatic para articular ossifications. In case of older bone injuries of a questionable nature also a check up on bone repair serial x ray studies in time intervals will clear up many diagnostic problems.

5. The confines of the field of roentgen diagnosis of fracture are not irremovably fixed. They change with the progress in roentgenological science and with the technical development of radiographic apparatus. The limitations of today denote the advances of tomorrow.

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# THE TREATMENT OF PERSISTENT RECURRENT BASAL CELL CARCINOMA OF THE FACE

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**B**ASAL cell carcinoma occurs most frequently on areas of the body not protected by clothing hence its most frequent location is on the face. It is a slow growing tumor which remains local. Since the lesions are on the surface of the body and in a place constantly inspected they are usually recognized and treated as early as any carcinoma of the body. This combination of circumstances early recognition easy access of therapy and slow growth without tendency to distant metastases moreover makes this one of the carcinomas most frequently cured.

In spite of these facts a small percentage of these growths recur. It can be fairly said that recurrence of a basal cell carcinoma usually means inadequate initial treatment. Whether excision irradiation local destruction with the cautery or electrocoagulation are used originally makes little difference. The choice of the method is not so important as the skill and thoroughness with which it is applied. These modes of therapy are all satisfactory if used sufficiently radically on adequate areas.

Unfortunately primary treatment is not always adequate. There are probably a number of reasons for this. These early lesions are regarded by many as having very little potential danger. It is well known that a high percentage of cures can be obtained and there is a certain squeamishness in most of us which causes hesitation in destroying tissue to the point where disfigurement results. These considerations and in some instances ignorance of the principles involved in efficiently using the therapeutic agent chosen tend to promote inadequate initial treatment.

The tendency to regard these lesions lightly is unfortunate for the initial opportunity is the golden one. Once a basal cell carcinoma recurs it is no longer a simple problem. However it is often regarded so and far too frequently a second small excision or a second

course of irradiation is prescribed for the patient following which the growth recurs rather promptly.

It is my opinion that once a basal cell carcinoma of the face has become persistent cure can oftentimes be effected only by destroying tissue of such magnitude that disfigurement results. It is much better to accept this view point and turn one's attention to ways in which to minimize or repair the damage necessary for cure than to continue temporizing.

Again it matters little in what way the wide destruction of the growth is accomplished so long as it is adequate. However if it is obvious that reconstruction will be necessary it is technically easier to effect repair if the lesion is surgically excised rather than destroyed by radiation. Following irradiation there is a certain amount of devitalization of tissue adjacent to the destroyed area which makes it difficult to get new tissue to grow satisfactorily when transferred. Then too the process of treatment is longer, with its attendant economic loss. Moreover irradiation alone of a growth once or twice recurrent following previous irradiation is not efficient. In such instances irradiation should be used only as a cautery would be used prior to surgical excision and repair. The cautery or electrocoagulation is a preferable agent for this purpose since it leaves tissue around the destroyed area in a more normal state. Cautery destruction of tissue prior to surgical excision is needed only occasionally. It is most useful in removing a sloughing or ulcerated and infected tumor in order to get a field for surgical excision which is not heavily infected.

I have gradually come to the conclusion that it is much safer to eradicate these recurrent persistent growths and repair immediately than is commonly thought.

This viewpoint is not in accord with the generally accepted teaching that the defect left should be kept open for inspection for 12 to 18 months, and, if recurrence does not take place in this period of time, repair should be carried out. In primary surgical removal of certain carcinomas about the face, this rule of leaving the defect open for observation has never been adhered to. For example, in carcinoma of the lip, even when extensive, immediate repair is usually done. The same holds true for small lesions about the face when closure by suture is possible. In general it might be said that, when the growth is deeply located, as for instance in the antrum, when bone or cartilage is involved, and particularly when the lesion is extensive or recurrent following previous irradiation or surgical excision, this belief that the wound should not be repaired at once has been the one usually held. I have a suspicion that subconscious doubt as to how to effect repair often enters into the decision to leave the wound open.

I agree that in primary surgical extirpations of certain tumors about the face, repair should be delayed. In general, deep invasive growths the complete eradication of which is doubtful, should not be repaired until one is certain that recurrence is not probable. However, large surface areas of growth should not be a deterrent to immediate repair if the surgeon has no lurking doubt in his mind that some cancer may have been left behind.

When a patient presents a persistent recurrent carcinoma of the face, the treatment should be radical surgery. Our plan at present is to examine the area carefully, determining as accurately as possible the surface involvement and estimating the depth of the tumor in its central or most active portion. In such a survey it must be remembered that recurrent basal cell carcinomas often extend outward under perfectly normal appearing skin. There is a characteristic thickened, slightly indurated feel to these, and the eradication must extend well outside this zone. If the growth is thought to be extending into bone, x-ray films of the region should be studied. Biopsy is useful in estimating the degree of malignancy. If the growth has an active fungating, necrotic center it may at

times be advisable to eradicate this area either with the cautery or by heavy irradiation limited to the central portion of the tumor. This, however, is done with the patient understanding that this is merely a preliminary step in the treatment and that radical surgery and repair will accompany or follow. This central destruction is done both to remove gross tumor and to produce a cleaner area for excision. If the cautery is used it often is combined with the first step of preparing material for repair.

During this examination one can draw a line about the tumor indicating its extent and about this another line, allowing a margin of one-half to one inch of good tissue. Such a procedure allows one to determine whether there is a possibility of primary closure or whether tissue must be brought from elsewhere to effect restoration. In no way must the margin of good tissue be sacrificed in order to make repair easier. It is better to err in removing too much rather than too little good along with the bad.

If the decision is made that tissue must be transplanted to restore that which must be removed, then plans are made *in advance* to meet this need.

This is a perfectly feasible method of handling persistent recurrent carcinoma of the face since in most instances the growth is restrained somewhat by the fibrous reaction to previous irradiation. Thus one has usually a demarcation of good tissue and tumor. If tissue is prepared for repair prior to excision of the growth, then at the time of excision the fresh wound can be repaired immediately. This prevents the necessity of long continued care of a large open lesion with its attendant economic loss. In some instances it may be possible to remove the tumor and carry out repair in one step. In the majority it will be necessary to prepare either tube grafts, delayed flaps, or a combination of the two prior to excision. These preliminary steps can often be carried out under local anesthesia without hospitalization. As soon as the condition of the tissue for repair is satisfactory, the patient is admitted to the hospital and radical excision of the growth and repair are carried out in one step. Some 4 to 6 weeks later, if a



pedicled transfer has been used the pedicle is removed under local anesthesia without hospital stay

This plan in the majority of instances entails one major operation with hospitalization and usually three minor steps without hospital stay. It enables one to remove the growth thoroughly without prolonged hospitalization or great economic loss due to inability to remain at work. Moreover it offers a fairly high percentage of long arrests of the tumor which in these persistent carcinomas is impossible to obtain by any other means now at our disposal

### CONCLUSIONS

The majority of basal cell carcinomas are at present treated initially by irradiation. This is an efficient method; it does not entail hospital expense in many instances the patient can continue at work and there is minimal disfigurement. However, once recurrence occurs following adequate primary irradiation or after presumably inadequate irradiation repeated on numerous occasions then radical surgical extirpation should be done.

In most instances these recurrent lesions can be satisfactorily eradicated by generously estimating in advance the amount of tissue which must be removed if necessary preparing the tissue for reconstruction beforehand then radically removing the lesion surgically and at the same time repairing the loss occasioned.

**CASE 1** M C S M H No 85 607 I first saw this 42 year old white married woman a doctor's secretary on October 26 1937. She wanted advice about a lesion in the skin of the left temporal region. About 7 years before at the age of 35 a small scaly lesion had appeared in this location. It had been treated by surgical diathermy and afterward by x-ray the amount unknown. About 2 years later the scar became raised and indurated and a scale would form repeatedly over it. At this time February 1934 treatment of 100 milligram hours of radium in contact with 1 millimeter of platinum filtration was given. In November 1936 about 2 years later the growth recurred. On this occasion she received 100 milligram hours with 1 millimeter of platinum filtration at 1 centimeter distance. In 11 months there was a recurrence and on this occasion October 26 1937 I saw her for the first time.

This young woman then had had her treatment by surgical diathermy and x-ray with recurrence con-

tact radium 100 milligram hours with recurrence and then 100 milligram hours radium at 1 centimeter distance with recurrence these 3 recurrences being during a period of roughly 7 years. During these years as far as I could determine a biopsy had never been done.

On examination in October 1937 there was found a small white scar in the left temporal region about 1 centimeter in diameter. Anterior and inferior to this there was an irregular induration of the skin for a distance of 2 centimeters. In one area there was a slight crusting of the skin.

The history and character of the lesion was compatible with a basal cell epithelioma. In view of the repeated recurrences following irradiation it seemed that wide surgical removal and repair was the best treatment and this was advised.

Accordingly on November 12 1937 the area was excised under local anesthesia all wing 1 centimeter of good tissue around the zone of infiltration going deeply under the growth and lifting it out in one piece. A full thickness free graft of skin from the abdomen was applied immediately. This took completely. Microscopic examination showed the lesion to be a basal cell epithelioma. She has been followed now for 2 years and as yet there is no evidence of recurrence. Her only complaint is that the graft is whiter than the surrounding skin. This could have been prevented by taking the graft from the postauricular regions or neck. However with the aid of dressing her hair judiciously and using cosmetics the blemish is not too unsightly.

**CASE 2** D M S M H No 10 056 This 60-year old Italian laborer was first admitted to the clinic of the Strong Memorial Hospital on April 30 1935. He complained of an ulceration of the right side of the nose which had first started about 15 years before. At first the lesion was slightly raised dry and bled occasionally. About 4 years prior to admission to the clinic the area was excised by his physician and he was given a few x-ray treatments. He had no trouble for about 18 months. The lesion then reappeared ulcerated and grew rapidly to about twice its original size. He returned to his physician and had one x-ray treatment but did not continue them because of expense. The ulceration continued to progress during the next 2 years without treatment. He then entered the clinic.

At that time an ulceration was present which had destroyed the skin and alar cartilages of the right side of the nose. The septum was exposed and around the ulcer there was a zone of inflammatory tissue which bled easily. The case was considerable purulent exudate.

General physical examination revealed a hypertension of 190-100 a cataract of the right eye general arteriosclerosis benign prostatic hypertrophy and a 4 plus Wassermann.

The right side of the nose was treated by giving a total of 100 r x-ray divided into 3 doses on three successive days. He was then followed in the outpatient department until June 1936. During this

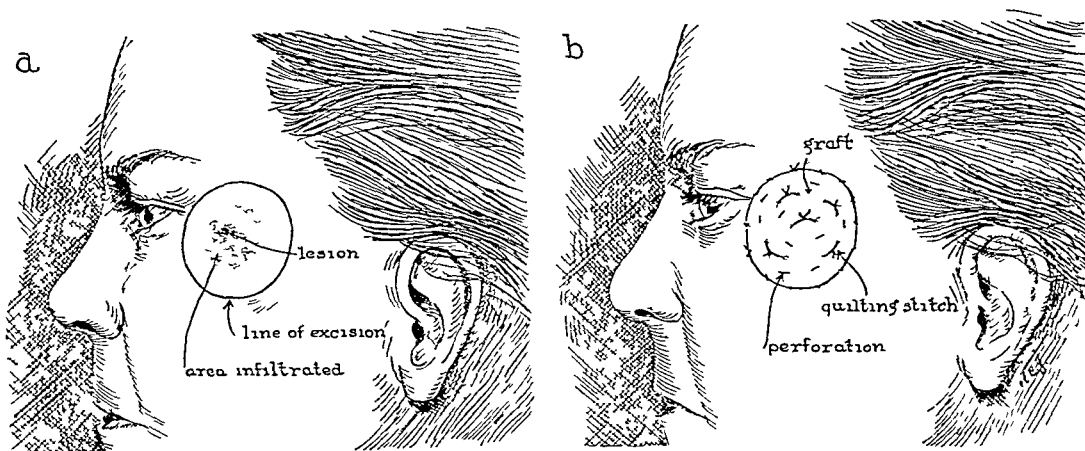


Fig 1 Case 1 a, Diagram showing extent of lesion under normal appearing skin b, Method of immediate

application of free full thickness skin graft, following surgical excision

time there was no evidence of recurrence, and the edges of the defect following slough from x-ray therapy gradually cleaned up and healed. During this period of time he received heavy antilutetic treatment.

On June 23, 1936, a forehead flap was partially elevated and delayed. On August 11 a second elevation of the flap was carried out. On August 25 elevation of the flap was completed. All 3 of these steps were done under local anesthesia. On September 17, 1936, the flap was judged to be in satisfactory condition for transfer, and on that date the margins of the defect were widely excised and the forehead flap was turned down into place. It had grown into place securely by October 6, 1936, and on this day the pedicle was returned to the forehead and the remaining defect was grafted with a split graft from the thigh. Both these steps were carried out under avertin plus ether anesthesia. Trimming operations on the reconstructed right half of the nose were done on January 7, 1937, and April 8, 1937, under local anesthesia.

This patient has been carefully followed and to date, approximately 4 years later, there has been no recurrence.

CASE 3 E H, S M H No 91,783 A 61-year old housewife entered the clinic June 22, 1938, because of the return of a "lump" in the right eyebrow. Eleven years before, she had what she thought was a small mole just above the right eyebrow which she picked with a pin. Two to 3 months later she noticed that the mole was becoming larger. She went to a physician who told her that she had a tumor about the size of a dime beneath the skin and removed it by fulguration. She then had no trouble for about 9 years. About 2 years ago she noticed that the scar above the eyebrow was enlarging and becoming lumpy. This enlargement has slowly but steadily increased. She has no other symptoms than the increase in size of the area above the eyebrow.

General examination showed that she had moderate arteriosclerosis and cardiac hypertrophy, but no other abnormalities than the growth above the right eyebrow.

There was a scar about 1 centimeter in diameter just above the middle of the right eyebrow. The center of this was slightly crusted, but not ulcerated. Extending outward from this scar was a firm subcutaneous thickening. This hardness extended under most of the eyebrow. The skin over it was perfectly normal. A biopsy was done and was diagnosed basal cell carcinoma.



Fig 1c Case 1 Basal cell carcinoma recurrent three times during 7 years. Left photograph shows condition present after third recurrence. Right photograph shows appearance of an off color free full thickness skin graft 1 year after surgical excision and repair. No recurrence to date (3 years).



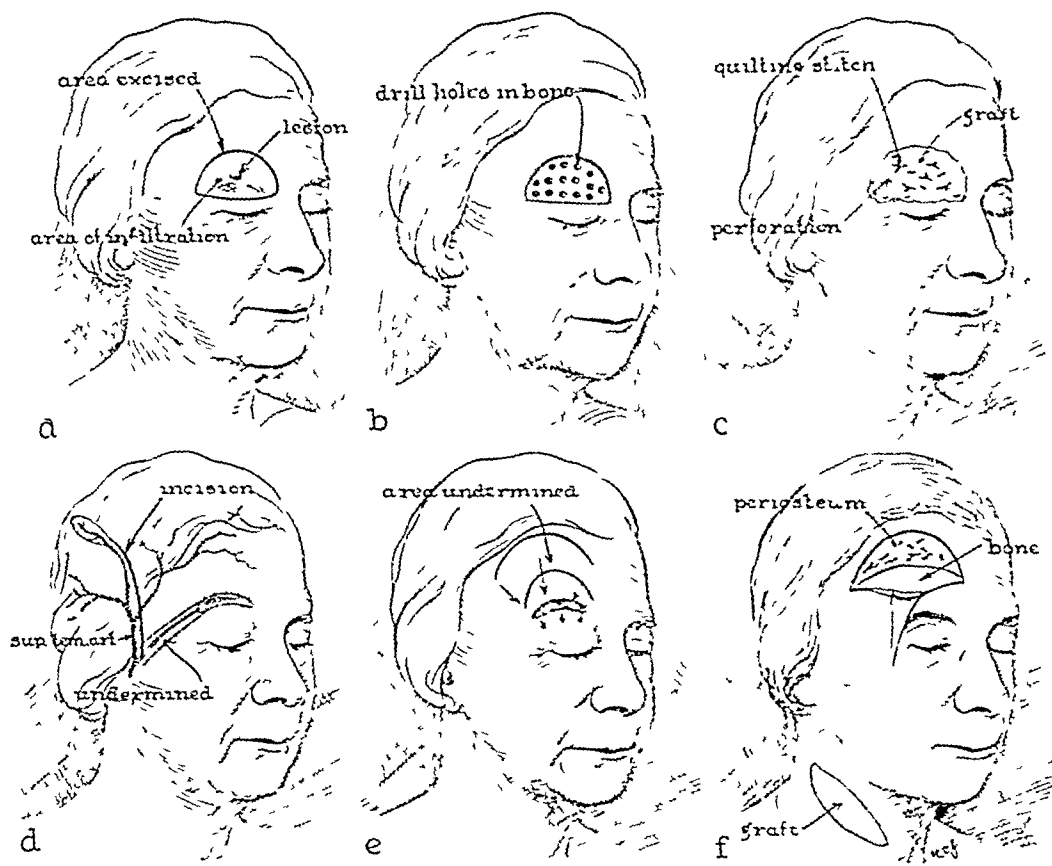


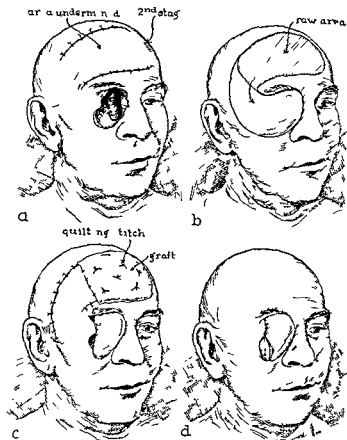
Fig 3



Fig 3g

Fig 3 Case 3 a, Diagram of extent of lesion, necessitating complete excision of eyebrow and surrounding skin down to skull, and, b, numerous drill holes in skull to allow granulations to grow up from cancellous bone c, Five weeks later granulating area epithelized with split thickness free skin graft from thigh d, Three months later eyebrow reconstructed by transplantation of temporal artery and vein carrying an attached piece of hair bearing tissue

from the scalp e, About 4 months later reconstructed eyebrow and adjacent skin slid downward, by undermining through incision just below hairline, to relieve tension on upper lid and, f, free full thickness graft taken from neck, used to close resulting gap of forehead skin below hairline  
 Fig 3g Case 3 Left photograph, granulating area after excision and bone drilling Right, 1 year after repair, eyebrow satisfactory, 2½ years to date without recurrence



Ft 4



Fg 4e

Fig 4 C sc 4 a Ex nteration forb t a d ethm d l gion be a se f b sal eff  
c rcin ma in ad n<sub>6</sub> bo y floor and med l wall forb t Two eeksl te l h d f p  
(Leg d e t d p p o t p g )

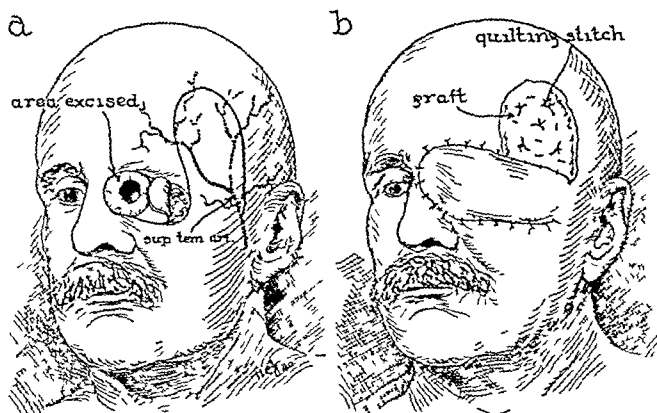


Fig 5 Case 5 a, Diagram showing extent of soft tissue and bone excised and flap of skin and subcutaneous tissue raised laterally and turned over to provide lining b, Forehead flap containing temporal vessels rotated for external skin and the site from which this came grafted with a split thickness graft When major vessel bearing flaps are obtainable, eradication and repair can be safely done in one step

growth contra-indicated radiation therapy In order to allow a satisfactory margin of good tissue about the growth, the entire eyebrow and the superior portion of the upper eyelid were removed down to the skull The bone was drilled in numerous places to permit granulations to form Thirty-five days later the bed of granulations was satisfactory and a split graft from the thigh was applied This took completely Three months later, after the graft had softened, the eyebrow was reconstructed by an arterial scalp pedicle graft A few hairs at the distal (medial) end of this were lost but the result on the whole was quite satisfactory However, after several months had passed, it was apparent that there was a tightness of the upper lid due to insufficient tissue and that the eyebrow was somewhat too high in relationship to the normal of the other side About  $4\frac{1}{2}$  months after restoration of the eyebrow, the final operative step was done An incision was made just below the hairline on the right side and a large flap of skin and frontalis muscle dissected free down to the upper eyelid In the upper portion the pericranium was left intact In the lower portion the graft adherent to bone was freed and the whole mass including eyebrow was slid downward A free full

delayed in two stages b, Four weeks later flap transferred and sutured to freshened edges of defect Forehead left to granulate c, Five weeks later, pedicle severed and rolled under to form defect lining, remainder of flap returned to forehead, rest of granulating forehead covered with one large split thickness skin graft d, Six weeks later lateral opening into defect closed in two layers, completing lining and covering

Fig 4e Case 4 Left photograph shows many times recurrent basal cell carcinoma which by x-ray had extended into bones of orbit Right photograph, result 2 years after repair No recurrence in 3 years



Fig 5c Case 5 Left photograph shows the sixth recurrence of a basal cell carcinoma on the nasal margin of a defect produced during previous treatment Right, result following surgical excision and closure carried out in one operation No recurrences to date, about 2 years afterwards

thickness graft from the neck was used to fill the gap just below the hairline This resulted in the necessary laxity of the upper eyelid and an improved lower position of the eyebrow The patient has been followed, and to date, 2 years after excision of the growth, there has been no recurrence of the growth

CASE 4 F N, S M H No 40,290 A white, male farmer first entered the clinic in October, 1930, because of a gastric ulcer for which gastric resection was done At that time a few small pearly nodules were present at the internal canthus of the right eye These were treated by x-ray, and the patient was given an appointment to return in 2 weeks for radium therapy For some reason this treatment was not given although he was seen quite frequently in the clinic for follow-up of his gastric status In August, 1933, he had an obvious recurrence of the rodent ulcer, and he was given 100 milligram hours of radium radiation The lesion recurred promptly

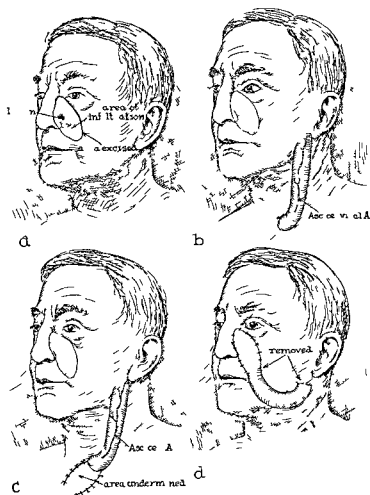


Fig 6



Fig 6e

(Le end pp 1 p 2)

and in January, 1934, it was destroyed by electro-coagulation.

Within 6 months the growth was again present. He was treated again by applications of radium. He did not appear in the clinic for about  $2\frac{1}{2}$  years. When seen at this time, August 17, 1937, there was recurrence of the growth with fixation to the inferior medial orbital rim. X-ray films of the region showed involvement of the infraorbital rim by tumor. It was decided that the only chance of arrest of the growth was by radical surgery, and I saw him for the first time on this occasion. An exenteration of the orbit along with the growth was advised. This was carried out in September, 1937. Two weeks afterward a large flap, with its pedicle including the frontal branches of the temporal artery, was delayed on the forehead. Three weeks later the distal end of the flap was cut across under local anesthesia. A week later the flap was transferred to the defect. Five weeks after the pedicle of the flap was divided and doubled under to line the inner surface of the flap with epithelium. The remainder of the pedicle was returned to the temporal region and the granulating area on the forehead grafted with a single split thickness skin graft.

These wounds all healed nicely and 6 weeks later the opening left laterally was closed. The patient was seen in June, 1939, approximately 2 years following removal of the tumor. At that time he complained of a bad odor in the nose and difficulty in getting rid of this. Intranasal examination showed that this was due to crusting and detritus in the large cavity under the repair. He was advised as to how to cleanse the cavity. There was no recurrence at that time.

CASE 5 F I, S M H No 34,006. A white, male laborer, aged 60 years, was first seen in the clinic in April, 1930, because of a growth in the region of the inner canthus of the left eye. This had been present for 5 years. During this time no treatment other than a protective dressing had been used. He complained that he had rather severe shooting pains in the growth and that it itched. At times it crusted over and seemed to him to be healing.

The growth was ulcerated, moist, red, and covered the entire left internal canthal area and most of the left side of the nose; the edges were rolled, and it was about the size of a silver dollar. The eyelids could be closed but could be opened only about one fourth of normal. There were no other abnormalities of consequence on general examination.

A biopsy was diagnosed as carcinoma of intermediate type. The sections were not typically squamous cell in type but seemed to be more malignant than the usual rodent ulcer.

Treatment was by unfiltered contact radium during the last 6 months of 1930. Approximately 300 milligram hours total of radium irradiation was given at about monthly intervals. The majority of the tumor healed but one small, apparently radio-resistant, area remained. This was removed by electrodesiccation in January, 1931. By the first of April, 1931, it was obvious that the growth had recurred. At this time a local excision of the recurrence was done. By September of this year, there was a probable recurrence which was treated by radium for 450 milligram hours. There was then no recurrence for a year, and the patient did not appear again in the clinic until August, 1933. At this time he had a small growth about 3 millimeters in diameter on the conjunctival aspect of the lower eyelid. He was treated with 40 milligram hours of radium and was to report in 6 weeks. He did not return, however, until about 1 year later, and he again had a large obvious recurrence. At this time the radiologist stated that he did not believe the growth could be controlled by radiation alone, but because surgery would have to be "extensive and mutilating," a maximum dose of radium was applied. The dose given was 8,225 milligram hours. In spite of this there was a persistence of the growth at the internal canthus and in October, 1935, about 1 year after the massive dose of radium, a subtotal exenteration of the orbit and eversion of the ethmoid cells were done. Following this he had no recurrence for a period of about 3 years. In December, 1938, he returned with an ulcer on the bridge of the nose which extended from the margin of the previous operative defect to the midline. In one area the ulcer edge was irregularly elevated, and a biopsy from this site showed basal cell carcinoma.

I first saw the patient at this time, and in going over the situation with the radiotherapist, we summarized the matter as follows: a proved basal cell carcinoma, recurrent numerous times over a period of 8 years, had been treated with a total of about 9000 milligram hours of radium and in spite of this treatment plus local surgery, carcinoma was still present. In view of these facts we both felt that further radiation was certainly not indicated. We therefore advised that a wide excision of the involved area and immediate repair be carried out.

In December, 1938, I excised the area and repaired it. This was accomplished by making an incision through good tissue about  $\frac{1}{2}$  inch beyond the ulcerated area down to bone. A corresponding rim of bone was removed attached to the soft tissues and the entire excised area lifted out in one piece. A flap of skin and subcutaneous tissue was then cut lateral to the defect with its pedicle near the direct margin. This flap was turned medially with its epithelial surface inward and sutured to small drill holes made in the nasal bone thus lining or the

Fig. 6 Case 6. a, Extent of infiltration of persistent basal cell carcinoma. b, Tubed flap formed on neck. c, Flap attached to tube delayed. d, Area outlined in a, excised and at once repaired with delayed flap, nourished by previously constructed tube graft. The nourishing tube after 2 months was excised and discarded.

Fig. 7 Case 6. Left photograph, indolent ulcer with wide zone of infiltration persistent in spite of radiation therapy. Right photograph, result after full thickness excision of soft tissues and repair. No recurrence in 5 years.



cavity was provided. The frontal branch of the temporal artery was not traced by palpation and a flap of skin and subcutaneous tissue was cut from the left temporal region just anterior to the hairline which included this vessel. This flap was turned downward over the raw surface of the lining flap and sutured to the edges of the defect. A split graft from the thigh was used to cover the raw area on the left temple. These flaps and the graft all took well and the patient's total hospital stay was only 27 days. Since that time to the present, roughly 2 years, he has been examined frequently and as yet there is no recurrence.

CASE 6 D S S M H No 67597. This 68 year old man first entered the clinic in September, 1933. At that time he had facial erysipelas which had started in an open wound in the left nasolabial fold. This wound the patient stated was due to a laceration received in an automobile accident 10 months previously which had never healed completely. On closer questioning it was found that he had had an indurated area with a dark center in the nasolabial fold for 10 years or more and that the so-called accidental laceration had more probably been a rupture of the area. It was also discovered that he had moderately severe diabetes. At that time it was thought that there might be a foreign body in the wound preventing its healing but due to the erysipelas exploration of the wound was postponed for 6 months.

In 6 months time as agreed he returned and at that time the lesion on the left cheek extended from the left internal canthus down the nasolabial fold to almost the corner of the mouth. It was quite indurated and about 2 centimeters wide. At about its midpoint there was a small ulcer. A biopsy examination of the ulcer edge was taken and found to be basal cell carcinoma.

Radiation therapy was started at once to the amount of 165 milligram hours. Felt red radium

was given. He was followed closely over a 3 year period. The induration never entirely subsided and during the last fall of the third year it was evident that the indurated area was spreading.

Because of the depth to which the induration seemed to extend it was decided that wide surgical excision offered the best chance of cure. I therefore planned to develop a tubed flap prior to excision and thus be able to remove the growth widely and to repair the loss at the same time. In October 1937 a vertical tube was constructed on the left side of the neck. About 1 month later a flap corresponding in shape to the area to be excised was developed at the lower end of the tube. This showed no vascular difficulties whatever and 3 days later the indurated area along with a 1/2 inch margin of normal tissue was excised in one piece. This block of tissue was peeled off the bone, all muscular tissue being removed along with the growth. The alar region the full thickness of the nose had to be removed to be safe. This left a small opening the edges of which were sutured in a somewhat makeshift manner. The chest end of the tube was then used completely to repair the defect. Sections of the removed block of tissue showed basal cell carcinoma invading the facial muscles.

After operation some infection developed under the flap. This cleared slowly under saline compresses and close attention to his diabetic regimen. Due to scar contracture following the infection the flap tended to bunch up rather than remain in flat position. About 2 months later the tube attachment was severed and by undermining the edges of the transplant the bulging was corrected. The remainder of the tube not used on the face was excised and discarded.

He has been followed now for approximately 3 years. There is a moderate asymptomatic enlargement of the left lower eyelid. The transplant has remained soft and as yet there is no evidence of recurrence.

# A FIVE YEAR SURVEY OF THE BLOOD SEDIMENTATION TEST IN ACUTE APPENDICITIS

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IN 1935 a paper on the blood sedimentation test and its value in the differential diagnosis of acute appendicitis was published by one of us. In this study it was observed that the blood sedimentation rate in acute appendicitis without rupture, whether catarrhal, suppurative, or gangrenous, was uniformly *normal*, whereas all other conditions producing the clinical picture of the acute surgical abdomen showed a definitely abnormal sedimentation reaction. In 1937 Bannick, Gregg,<sup>1</sup> and Guernsey published a confirmation of our observation based upon a 2 year survey of acute appendicitis at the Mayo Clinic.

We are now submitting a supplementary report on the blood sedimentation test in a series of cases in which patients were operated upon for acute appendiceal pathology, in the 5 year period from 1935 to 1939. This present series of cases, like the original group, was studied at the Metropolitan Hospital, and the same gradations of readings, as previously established by the Westergren technique, were used, as follows: 6 millimeters to 15 millimeters in the hour, normal reaction, 25 millimeters to 40 millimeters in the hour, moderate reaction, 60 millimeters to 80 millimeters in the hour, high reaction, 80 millimeters to 140 millimeters in the hour, severe reaction. For purposes of simplification the technique of the Westergren method was slightly modified so that 4 cubic centimeters of blood was added to a test-tube containing 1 cubic centimeter of 3.8 per cent solution of sodium citrate. There was one circumstance in the performance of the tests, however, that differed from conditions existing in the original study: since sedimentation tests had become routine procedure for acute surgical admissions, they were performed by a large number of individual internes each of

whom spent a relatively short time on the surgical service during their rotating internship. The results represent, therefore, a measure of the average accuracy of technique of a fairly large number of individuals rather than the constant degree of accuracy of one or two individuals (in the original study all tests were performed by the authors).

This report presents 132 cases of patients operated upon with a preoperative diagnosis of acute appendicitis or primary appendicular pathology. In 15 of these cases the preoperative diagnosis was erroneous, operation revealing pathological condition other than appendicitis. As demonstrated in the original report, the conditions most commonly responsible for confusion with acute appendicitis were acute salpingo-oophoritis, acute inflammatory chest conditions, tuberculosis—pleural or abdominal—pyelitis, mesenteric adenitis, and acute rheumatic fever. In these 15 extra-appendiceal conditions the sedimentation readings were consistently elevated or high, as differentiated from the normal readings found in acute appendicitis. In 8 cases there were complicating appendiceal abscesses, and in 10 cases there were found generalizing peritonitis of varying degree and severity. Again it was noted, as in the original study, that all cases complicated by abdominal abscess or peritonitis showed a consistently elevated blood sedimentation rate varying from high to severe reaction.

In 99 cases the preoperative diagnosis of acute appendicitis was verified by the operative findings, revealing an acute catarrhal, suppurative, or gangrenous appendix. In 90 of these cases the blood sedimentation rates were 15 millimeters, or less, in the hour, that is, within the absolute normal as previously established. In 9 cases the blood sedimentation rates were slightly above 15, the readings varying from 21 to 26 millimeters in the hour. We believe that this very slight deviation

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from the absolute normal in a small percentage of cases may be explained by minor inaccuracies or deviations from precise detail of technique on the part of the large number of internes called upon to perform these blood sedimentation tests as a routine of the admission work up. Such minor inaccuracies of detail may consist of inexact proportions of blood and sodium citrate, lack of proper cleanliness of the sedimentation tubes and prolonged standing of the citrated blood before performing the test. We offer this explanation only to stress the fact that these tests were performed not by a small number of laboratory technicians but rather by many first year internes in whom slight inconsistencies of laboratory technique may be expected.

#### SUMMARY

1 The routine use of the blood sedimentation test has contributed to the more accurate differential diagnosis of the acute surgical abdomen and particularly of acute appendicitis.

A consistently normal blood sedimentation rate in acute appendicitis has been corroborated in more than 90 per cent of cases in a survey covering a 5 year period.

3 A small percentage of cases show a slight elevation from absolute normal. This circum-

stance may be due to minor deviation from details of technique as a result of routine ward usage and in any event does not affect or alter the significance of a low or minimal blood sedimentation rate in all cases of acute appendicitis.

4 Acute adnexal disease, the condition most commonly to be differentiated from acute appendicitis in acute abdominal cases routinely admitted to the surgical service of a large municipal hospital, has come to needless and frequently harmful operation much less frequently as a result of increasing awareness of the blood sedimentation test.

5 As previously observed, there is no relationship between leucocytosis and the blood sedimentation reaction.

6 This survey of cases over a 5 year period further substantiates the importance of the blood sedimentation test in the differential diagnosis of acute appendicitis and warrants its continued use and clinical application.

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# OCCURRENCE OF POSTOPERATIVE ACIDOSIS AND PAGETOID BONE CHANGES IN HYPERPARATHYROIDISM

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TWO cases of parathyroid tumor associated with hyperparathyroidism are presented with a discussion of two important and as yet unstressed aspects of this syndrome. One case brings out clearly the dangers of acidosis in such cases, and it presents as well many of the factors which make these cases difficult to diagnose and to treat. The other case illustrates a rare and easily missed type in which the skeletal lesions in many ways resemble those of Paget's disease.

The occurrence of acidosis as a sequela of parathyroidectomy in hyperparathyroidism is probably not rare and when it does appear is a very dangerous complication. Though there are many accounts of anuria, terminal nephritis, and uremia, associated with the various kidney lesions in the disease, little has been said about retention of acid radicals in, or the loss of the alkaline radicals from, the acid-base neutralizing mechanism of the body (1, 2, 7, 8, 9). This mechanism as well as its relation to acidosis in patients after parathyroidectomy is discussed, in an attempt to explain the cause of the acidosis and to outline certain pre-operative and postoperative measures for its prevention.

Pagetoid bone changes associated with a hyperfunctioning parathyroid adenoma have been described infrequently in the literature (3, 6). Though in hyperparathyroidism decalcification is usually steadily progressive and widespread, at times it seems that it progresses more rapidly in one bone than another, and again there may be periods of quiescence or even recalcification. Such episodes simulate Paget's disease in an x-ray study of the skeleton. In the cases of Gutman and Parsons, Paget's disease actually did play a part, but in the case here reported there had never been any indication of Paget's disease other than the simulation in the roentgenograms.

## CASE REPORTS

The first case illustrates the difficulties surrounding the diagnosis of parathyroid adenoma associated with hyperparathyroidism, the difficulties and the methods of finding such a tumor at operation, the dangers attendant on, and the treatment of, the postoperative chemical disturbances, and the happy culmination to be expected following successful treatment.

The signs and symptoms of hyperparathyroidism are conveniently divided into three groups: (1) those which relate to the presence of hypercalcemia, briefly, depression of all neuromuscular functions, (2) those due to loss of calcium from the skeleton, namely, generalized rarefaction of bones, (3) those due to a damaged kidney, called upon to excrete a heavy load of calcium daily, for example, impaired kidney function, renal metastatic calcification, nephrolithiasis, or acidosis.

The patient in Case 1 followed these in turn.

**CASE 1.** Mrs. B., aged 52 years, was admitted to Toronto General Hospital, May, 1939, complaining of increasing lassitude, muscular weakness, loss of appetite, and a loss of 50 pounds in weight. Physical examination showed cachexia, and achlorhydria with a hemoglobin of only 30 per cent. Although this group of symptoms and signs was probably due to a high serum calcium level it was not sufficient to lead to the true diagnosis.

The patient improved on iron and was sent home for 6 weeks. She then showed the second group of signs, namely, that due to loss of calcium from the skeleton. Her bones had lost so much calcium that she suffered a fracture of the femur. On readmission to hospital, it was noted that her skull could be dented like rubber and her ribs fell in instead of lifting on inspiration.

Blood chemical studies showed serum calcium increased to twice normal, serum phosphorus decreased to half normal, phosphatase increased to four times normal (Table I and Figs. 1 and 2).

A detailed study of calcium balance, carried out by the Department of Medicine at the Toronto General Hospital, proved that, on ordinary diet, the patient was excreting five times the amount of cal-

TABLE L—PARTIAL SERUM CALCIUM PHOSPHORUS PHOSPHATASE AND CALCIUM METABOLISM—CASE I Mrs B

Preoperative											
Patient	Date	Vit. m	Vit. h	U. l. m	fecal	Calc. m	Calc. m	C. l. m	S. m	S. m	Phos. p. hase
	6-8-33	43		36	3	366	47	-59	6	8	K 75
CO C P 40% 4% 1											
3	6-4	390	7	45	7	56	87	-75	43	9	
5	6-3	8	8	39	7	6	88	-33	5	7	5
7	2-6	33		67	4	67	3	+56	49	8	5
	2-9										
At the end of											
Postoperative											
	7-3								6		5
	4								7		56
	7-5								65	47	
	7-6								63	45	7
	7-7								7	43	8
	7-8								76	4	3
	7-5	466	3	35		65	37	+8	85		5
7	8-9	85	6	5	367		7	+95	8	39	9
	8-5										
At the end of											
1	2-6	84	63	6			73	+363		33	4
	6-9										
35	6	86	33	3	88	37	69	+55	97	34	
	2-6										
V. l. d											
38	3-8	775	55	5	5	667	700	+633	95	36	
	3-9										
O. p. l. l. f. w. k											
44	5-7	57	96	55	97	5	667	+65	6	33	
	5-8										
O. cap. l. califer. l. sm. th											

cium sh. was imbibing each day the excess being removed from the skeleton (Table I). Roentgenograms of the skeleton revealed widespread and advanced rarefaction and multitudes of tiny bone cysts besides one large cyst at the site of fracture (Fig. 3). A biopsy specimen of bone was taken from the fracture site and a diagnosis of osteitis fibrosa cystica made. Kidney function tests before operation showed a specific gravity range of 1.009-1.024 and again 1.010-1.013 with day and night urine excretion amounts almost equal the first time and the day urine volume twice the night urine volume the second time. Nonprotein nitrogen in the blood before operation ranged from 43 to 47 milligrams per cent. Carbon dioxide combining power of the blood ranged from 40 to 47 volumes per cent before operation.

Blood sodium before operation was 268 milligrams per cent.

The diagnosis of hyperparathyroidism was therefore established with surety by the finding of a consistently elevated serum calcium, a consistently low serum phosphorus, a consistently high phosphatase reading, a persistently negative calcium balance, diffuse skeletal decalcification and a biopsy of bone tissue confirming the presence of osteitis fibrosa cystica (3-6). It remained then the surgeon's task to complete the clinical picture by finding the tumor. It was borne in mind that more than one patient has been operated on repeatedly because removal of unconfirmed tissue or no mal parathyroid tissue failed to relieve the symptoms and that each operation is attended with a definite risk. Therefore the

plan was followed of searching the usual sites first—the easily explored areas around the thyroid gland second, and then the thyroid gland itself before contemplating the potentially dangerous maneuver of retrosternal examination.

The tumor was not visible or palpable on exposure of the thyroid area, and biopsy of numerous superficial and suspicious thyroid nodules did not reveal a parathyroid tumor. The region around the thyroid from hyoid to sternum was thoroughly examined, the prevertebral fascia being opened also. No tumor was evident. Therefore the right thyroid lobe was resected and examined in the gross and by quick section by the pathologist. As no parathyroid tumor was found, the left lobe was resected, and finally the tumor was discovered completely imbedded in thyroid tissue. Operation was not prolonged in spite of these difficulties and the patient was returned to bed in good condition (Fig. 4). Microscopic examination showed the tumor to be composed of cords and irregular masses of oxyphil cells (Fig. 5).

Ten hours after operation the patient manifested the third group of symptoms mentioned, that associated with acidosis. Breathing suddenly commenced to become more rapid and shallow, the pulse rate mounted quickly, the blood pressure was increased to 160/70 millimeters of mercury. The patient soon became unconscious. Carbon dioxide combining power was found then to be only 19 volumes per cent. The blood chloride estimation was 800 milligrams per cent. There was no evidence of tetany. Blood serum 5 hours after operation had shown a calcium of 12.6 milligrams per cent, phosphorus of 2.1 milligrams per cent, and a phosphatase of 50 units (Kay). Surgical shock was not present.

To combat this condition 500 cubic centimeters of 5 per cent sodium bicarbonate in distilled water was given slowly intravenously and in 1 hour the patient was again conscious, fairly bright, with a pulse of 100 and normal respirations. A carbon-dioxide combining power determination done a few hours after recovery read at 56 volumes per cent, while later in the first day after operation it was 60 volumes per cent. The blood chloride estimation a few hours after recovery from acidosis, was 575 milligrams per cent. The nonprotein-nitrogen of the blood was 54 and 47 milligrams per cent the day after operation.

No recurrence of acidosis threatened. The carbon dioxide combining power remained between 52 and 57 per cent, by volume, for the first week after operation and during the next few months ranged from 45 to 67 volumes per cent. Nonprotein-nitrogen estimations varied between 32 and 57 milligrams per cent. Four days after operation the blood sodium reading was 299 milligrams per cent, while 10 days afterward it was read at 350 milligrams per cent.

There was a variable and barely noticeable Chvostek's sign present on the second postoperative day when the serum estimations were calcium 6.5, phosphorus 4.7 milligrams per cent. This sign was occasionally present until the tenth postoperative day during which time calcium lactate and ditachy-

sterol were given and continued thereafter. As shown in Table I the serum calcium ranged during this time from 6.5 to 8.5, while phosphorus ranged from 4.7 to 10 milligrams per cent.

The patient's progress was very satisfactory from the first day after operation. Besides a return to normal serum calcium and phosphorus content, the phosphatase reaction more gradually returned to normal (Table I Figs. 1 and 2). The patient's melancholia disappeared entirely. Her cachexia rapidly vanished. Her fractured femur progressed to union gradually. Roentgenograms a year after operation showed progressing recalcification of all bones, although the femora still showed some areas of cyst formation (Fig. 3).

The second case illustrates how, in hyperparathyroidism the bony changes may simulate those of Paget's disease.

CASE 2. Mrs. McK., aged 64 years, was admitted to St. Joseph's Hospital, Toronto, April 10, 1930. She had fallen on her right hip earlier in April, 1930. Though bruised slightly she carried on for several weeks when her physician suggested that x-ray study was advisable because of the continuing soreness in hip and of a long continued aching pain in both lower limbs. Examination prior to the x-ray study revealed only slight tenderness over the right greater trochanter and questionable limitation of movement of the right hip joint. An x-ray film of the affected hip was reported as showing the changes of osteitis fibrosa cystica (Fig. 6). Besides the bone cysts there could also be noted some lying down or new bone beneath the cortex of the femur, particularly in several parts of the pelvis. With this film in mind the patient was then re-examined. A story of aching bones, with loss of about 3 inches in height without much change in hat size in several years, gradually increasing muscular weakness, general wasting, the loss of 30 pounds weight in a few years with loss of appetite and bouts of nausea and constipation, along with a tumor in the right lower neck anteriorly, made one suspicious of the presence of hyperparathyroidism, and the patient was admitted for investigation.

Further study of the patient in the hospital elicited the following facts. For many years she had had infrequent exacerbations of rheumatic heart disease with several periods of cardiac insufficiency. Mitral stenosis was present. There was no day or night frequency of urination or other evidence of kidney failure in the patient's history. Routine urine and kidney function tests revealed a variation in the urine's specific gravity, between 1003 and 1012, with a fair, though slightly altered, balance between day and night volumes. Nonprotein-nitrogen determinations varied within normal limits. Carbon dioxide combining power estimations indicated a normal alkaline reserve.

Additional x-ray films taken in the hospital showed decalcification of all the long bones, and decalcifica-

# SURGERY GYNECOLOGY AND OBSTETRICS

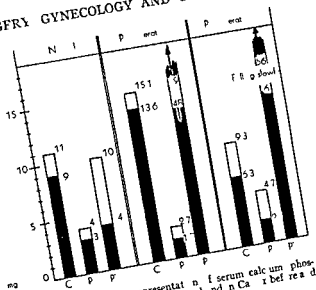


Fig 1 Diagram representing phosphorus and phosphatase figures before and after parathyroidectomy

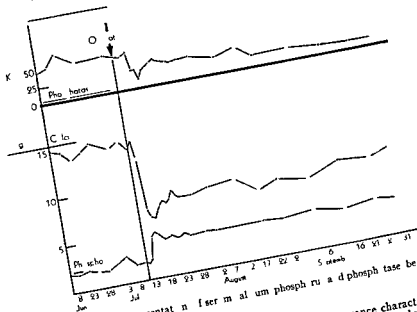


Fig 2 Graph representing the course of phosphorus, calcium, and phosphatase before and after parathyroidectomy

tion of the spine but no vertebra was actually collapsed. No bone cysts were present except in the pelvis and the femora. The skull roentgenogram was typical of many others taken in cases of hyperparathyroidism. There were widespread areas of decalcification without regions of recurrent bone deposition and without the

cotton wool appearance characteristic of Paget's disease. Thickening of the cranial vault with separation of the outer and inner tables was also seen as is common in hyperparathyroidism. Chemical investigations were carried out by Mr Wakefield at the Toronto General Hospital and by Dr Farquharson and Mr Simmons of the Depart-

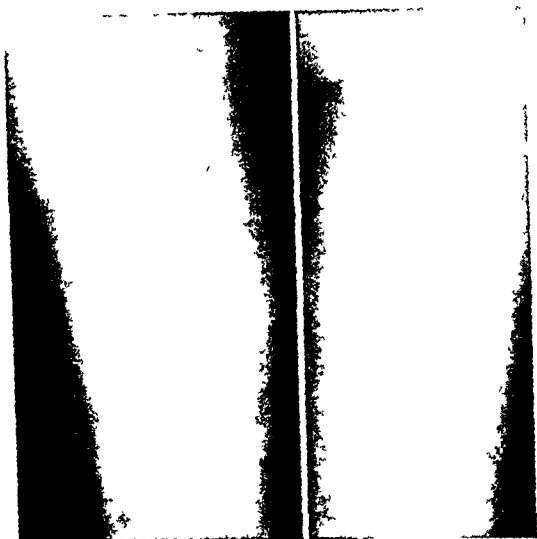


Fig 3 Roentgenograms of left femur of Mrs. B., Case 1, 2 months before and 8 months after parathyroidectomy

ment of Medicine, University of Toronto. A constantly elevated serum calcium content and phosphatase reaction were present with a lowered serum phosphorus content. On a low calcium intake diet the patient constantly maintained a negative calcium balance (Table II, Fig 7).

These data in conjunction with the history and physical findings, including the lump in the right neck, pointed strongly to a diagnosis of parathyroid tumor causing hyperparathyroidism.

For a week prior to operation a high calcium intake diet, along with viosterol, was given, in an attempt relatively to reduce the calcium loss from the body. The efficacy of such treatment is perhaps not too well proved and some think it may lead occasionally to calcification of tissues, particularly renal tissues. Also, for some time prior to operation, the patient was placed on a salt free diet in order to guard against possible acidotic, nephritic, and cardiac complications.

Operation was done under local anesthesia in order to minimize the operative risk. A large tumor 3 by 2 by 1.5 was found easily, lying a little posterior to the right lower thyroid pole. The tumor was outside the thyroid capsule, was grayish white in color, and was lobulated (Fig 8). It was supplied by a small branch of the inferior thyroid artery. Quick section confirmed the gross pathological diagnosis. No other tumors were noted.

Microscopic examination of the specimen revealed fairly typical parathyroid tumor tissue of the primary type. Acinar arrangement was common but many long strands of cells were also seen. Scattered oxyphil cells and large water-clear cells were present (Fig 9).



Fig 4 Left thyroid lobe with parathyroid tumor imbedded in pole in Case 1

The postoperative course was quite uneventful. Patient was up and about the second day. There was no evidence of tetany, acidosis, or of kidney failure. The blood chemical changes and the calcium balance changes were quite normal for such a patient, the serum calcium and phosphorus becoming rapidly normal and the phosphatase reaction gradually returning to a normal level. Measurement of urine calcium excretion indicated a positive calcium balance (Table II, Fig 7), postoperative roentgenograms, rapid laying down of calcium in bones with obliteration of areas of cyst formation (Fig 10).

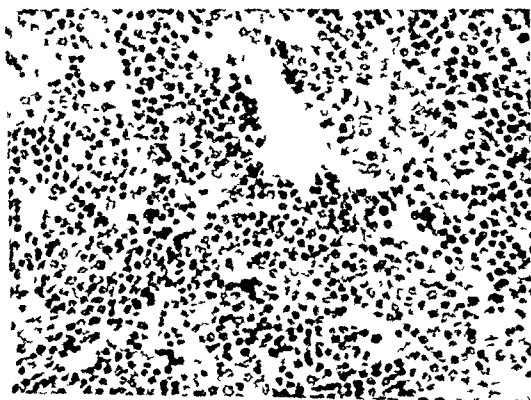


Fig 5 Photomicrograph of section from parathyroid adenoma in Case 1



SURGERY GYNCOLOGY AND OBSTETRICS

	Fe c m	Calci p	C to m t	C ium b la	m ic m	Serum phosphorus
TABLE II—SERUM CALCIUM PHOSPHORUS PHOSPHATASE CASE 1 Mrs McK						

[illegible]

The first case report that of Mrs B brings out only too clearly the suddenness with which the factor of acidosis may alter the entire outlook in hyperparathyroidism. In this case if the situation had not been immediately recognized and combated an unhappy ending would have been the only reward for much work and skill. From a review of the literature it is difficult to estimate the frequency of acidosis as a complication. There is reason to believe however that it is relatively common and that it is associated with a high mortality.

In attempting to discover the causes of acidosis in such cases one almost at once seeks an answer in the damaged kidney function displayed by so many of these patients. A large number of such patients suffer from nephrolithiasis renal calcification or tubular

and glomerular nephritis. Excretory and blood tests frequently indicate a greatly diminished kidney function. Despite this fact but few of the case reports indicate that the patient suffers from acidosis in fact it would appear that excretory tests and the usual blood tests for renal function do not give any indication of the patient's liability to acidosis. In Case 1 renal excretion was impaired blood nonprotein nitrogen was slightly above normal and the carbon dioxide combining power of the blood was lower than the usual level. Many another such patient however has exhibited more marked impairment of renal function and yet did not develop the complication of postoperative acidosis. Even patients with marked renal calcification have weathered operation successfully and anuria or

suddenly increased malfunction has been the usual complications (7). It is interesting in this regard that Mrs B (Case 1) had the acidotic sequela but no tendency to anuria or further impairment of kidney function.

It seemed reasonable then to look elsewhere for an explanation of this variety of acidosis. From the data at hand, it would appear that shortly after operation the alkali reserve, as measured by the carbon dioxide combining power of the blood, became lowered markedly within a few hours. This must have come about through an alteration in the tissues or blood stream as no intestinal disturbance and no medication entered as a factor. The figures for nonprotein-nitrogen and the kidney function, as mentioned, did not hint at ordinary renal retention as an important factor. Examination of the changes in blood calcium and phosphorus after parathyroidectomy in hyperparathyroidism, and the effect of these changes on other factors in acid-base equilibrium, appears then the most logical source of information.

Before proceeding further into this, however, a brief summary of the recent ideas on the interfunctions of calcium, phosphorus, and parathormone is indicated. Helfet has recently clearly pictured parathormone controlling the blood inorganic phosphate level by stimulating the kidney to excrete more phos-



Fig 6 Roentgenogram of pelvis and femora in Case 2, Mrs McK, taken 2 months before parathyroidectomy.

phates when they increase in the blood, and by mobilizing calcium from the bones to form salts which either hold the phosphates in the blood stream or allow their excretion by the kidney. Conversely, if parathormone is removed from the body, phosphate excretion is impaired and calcium is no longer mobilized from bone either to help its excretion or to hold it in the blood stream in a neutral form (5).

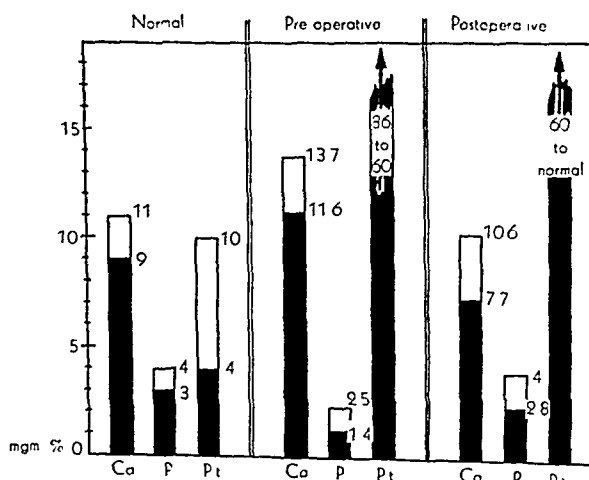


Fig 7 Diagrammatic representation of serum calcium, phosphorus, and phosphatase figures in normal and in Case 2, Mrs McK, before and after parathyroidectomy.



Fig. 8. Photomicrograph of parathyroid gland, Case 2, Mrs. McK.

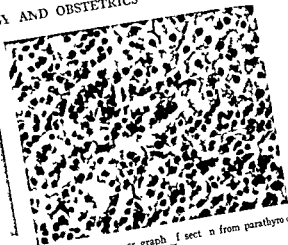


Fig. 9. Photomicrograph of section from parathyroid gland, Case 2, Mrs. McK.

With this in mind it is further recalled that a kidney with impaired function tends to excrete certain acid radicals poorly especially chlorides and sulphates. This seems to be especially true in hyperparathyroidism and in this syndrome phosphates are also excreted with difficulty in spite of increased parathormone. Calcium though certainly excreted in immense quantities by the kidney tends to lodge in the soft tissues. Sodium is excreted freely (10).

The removal then of a hyperfunctioning parathyroid gland invites immediate chemical changes of great importance. With the loss of parathormone phosphates no longer tend to be excreted by the kidney and increase while the calcium that was mobilized from bone to take care of it no longer is freed. Therefore the phosphates sulphates and chlorides all acid radicals tend to increase in the blood stream or in the tissues while calcium a base is no longer withdrawn from the skeleton to the blood stream and the base sodium is excreted by the kidney. A process is thus set in motion that may prove sufficiently disturbing to the acid base equilibrium to promote acidosis.

In Case 1, Mrs. B. some impairment of renal function was present before operation. Carbon dioxide combining power was slightly

down. Calcium was increased in the blood stream. Phosphorus was decreased in the blood stream. A few hours after operation serum calcium was 12.6 milligram per cent. Phosphorus 2.1 milligram per cent and the patient was in good condition. But 10 hours after operation when acidosis had suddenly developed carbon dioxide combining power had fallen as low as 19 volumes per cent. A few hours after recovery from acidosis serum calcium was 7.1 milligram per cent. Phosphorus 3.1 milligram per cent. It seems reasonable to suppose that with the withdrawal of parathormone by operation phosphates were retained in the body while due to the kidney damage sulphates and chlorides already tended to be retained. Thus acid radicals were increased while at the same time sodium was freely excreted and calcium was retained in the body not in the blood stream available to counteract acid radicals but in bone. Thus in acid radicals were depleted leading to a depleted alkaline reserve and to acidosis.

The treatment of the acidosis by intravenous sodium bicarbonate was immediately and dramatically effective. The lowered carbon dioxide combining power changed to a normal level indicating a supplementing of the alkaline reserves sufficient to offset the increased acid radicals. Besides being effective sodium bicarbonate is a very safe agent to use to combat acidosis of this type for the sodium if necessary is readily excreted by the

kidney while carbon dioxide is freely excreted by the lung. There is, therefore, no danger of overtreatment within reasonable limits.

A salt free diet, for a week or so before parathyroidectomy, would seem to be a logical preventative measure in these cases.

Before leaving the discussion of Case 1, it should be pointed out that the very mechanism here outlined that may lead to acidosis with rapidity may also lead to hypocalcemic tetany. When parathormone is no longer available after operation, calcium is no longer drawn from bone; and that calcium still in the blood stream is rapidly attached, diffusible calcium being rapidly used up. Thus tetany may appear with acidosis, render the patient's position precarious, and make a diagnosis of the exact condition even more difficult.

The second case reported here had diffuse rarefaction of the skeleton, but rarefaction was not evenly distributed. Bone cysts were present in the pelvis and femora but not in the other long bones. In the pelvis and femora, areas of calcium deposition were present. These areas in the x-ray film bore a strong resemblance to the changes seen in the roentgenogram in Paget's disease. However, the findings in the case and the postoperative course definitely established the diagnosis of hyperparathyroidism due to a hyperfunctioning parathyroid adenoma. Gutman and Parsons believe that this unusual picture is explained by the fact that hyperparathyroidism progresses often in phases. For a time much parathormone excretion results in much decalcification of bone; then decreased parathormone excretion brings about a period of recalcification of bone, usually in an uneven manner. The presence of areas of bone deposition together with bone rarefaction and bone cysts is thus accounted for.

The realization of such a possible variation in the bone pathology of hyperparathyroidism is important because such an x-ray picture as Mrs. McK. presented might lead one away from the true diagnosis. This would be especially true if by chance blood tests for calcium and phosphorus and phosphatase were taken at a time when parathormone activity was quiescent, rendering the tests within, or almost, within normal limits.



Fig. 10. Roentgenogram of pelvis and femora in Case 2, Mrs. McK., taken 4 months after parathyroidectomy.

#### SUMMARY

Two cases of hyperparathyroidism, due to the hyperactivity of parathyroid adenomas, have been reported. One emphasizes the importance of watching for postoperative acidosis, its grave dangers, and its effective treatment by intravenous sodium bicarbonate. It is also emphasized that acidosis and tetany may occur together. Cases must be carefully watched for both conditions, either of which may be fatal. An explanation is given for the occurrence of the acidosis following parathyroidectomy; briefly that acid radicals such as phosphates, sulphates, and chlorides tend to be retained in the blood stream while the base sodium is excreted freely by the kidneys and the base calcium is retained in the bones. A tendency for acid radicals to increase over basic radicals is thus present.

The other case illustrates how the skeletal changes shown in the x-ray film in hyperparathyroidism may closely resemble those of Paget's disease. It is pointed out that exacerbations and remissions of parathyroid activity could give this picture, bone being decalcified at one time and recalcified at another. Cases of Paget's disease should be carefully investigated with this circumstance in mind.

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# THE CONTRACTILE RESPONSE OF THE HUMAN UTERUS TO POSTERIOR PITUITARY EXTRACT ADMINISTERED AT REGULAR INTERVALS DURING PREGNANCY

A Study of 32 Patients with the Lóránd Tocograph

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THE Gyneccean Hospital Institute of Gynecologic Research recently has undertaken an investigation of the contractions which the human uterus undergoes during pregnancy. This has included observations upon both the spontaneous ones (2), and upon those induced by the administration of posterior pituitary extract (3).

The latter study supplied information upon the general character of the response and on the effect of certain factors upon it. It told nothing, however, about the peculiarities of a given individual's total reaction throughout pregnancy, or in what manner the response of one person during gestation might differ from that of another. These deficiencies were due primarily to the small number of observations made upon any one patient as well as to certain variables inherent in the nature of the material. The present study was undertaken in order to throw light upon these subjects, and as far as can be determined no similar series of observations has been reported.

## MATERIALS AND METHODS

Patients residing in the Sheltering Arms Home, Philadelphia, between June, 1939, and June, 1940, acted as subjects. This institution affords residence and prenatal care only, beginning at any time during pregnancy, for white and colored women who are illegitimately pregnant.

Each patient was brought under observation within 7 days of admission to the Home and was studied at weekly intervals thereafter. All records were made on the same day

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and hour of each week, when possible. Each observation period included a record of uterine contractions, and while these were being registered the patient received a dose of obstetrical pituitrin,<sup>1</sup> which was administered intramuscularly in the upper arm. The dose of pituitrin was the same each week during the entire period that the patient was under observation.

Doses of 1 minim were employed when the study was started. Since this amount failed to elicit a response in many instances, the dose was increased but was limited to 3 minims, because even this quantity caused discomfort to some patients.

The latest model tocograph (1) was used for the recording. This instrument, 3.0 by 8.0 by 6.5 centimeters in dimensions, is a mechanical device which registers upon a paper strip the change in the contour of the abdominal wall created by the change in contour of the underlying uterus when it contracts. The tocograph supplies data upon the incidence, strength, duration, and rhythmicity of the uterine movements. The technique of the recording was as follows: The patient rested upon her bed for 10 minutes. The tocograph was then placed upon the most prominent part of her abdomen in the midline, where it was secured with a belt, and spontaneous uterine activity was registered for a control period of 15 minutes. Without interrupting the recording, pituitrin was administered, the period of observation being continued for the following 30 minutes.

## RESULTS

A series of 32 patients supplied the data forming the basis for the present report. The

<sup>1</sup> Parke, Davis & Co.

SURGERY, GYNECOLOGY AND OBSTETRICS

TABLE I—CONTRACTILE RESPONSE OF PREGNANT HUMAN UTERUS TO POSTERIOR PITUITARY EXTRACT

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SURGERY, GYNECOLOGY AND OBSTETRICS

TABLE I—CONTRACTILE RESPONSE OF PREGNANT HUMAN UTERUS TO PITUITARY EXTRACT

Dosage in minims

30

Totals

Treatments

10 15 20

Patient identification

Weeks of gestation

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32

16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32

(+) = Response  
(-) = No response

(a) Absence of any response on the part of patients 4 and 21  
(b) Absence of response of remaining patients at 4th week of gestation  
(c) Increasing frequency of response as pregnancy advances  
(d) Greater response than the smaller doses of pituitary

Table I also show that the frequency of response increased as pregnancy advanced. The differences in the response of the patients are shown in the following table:

(+) = Response  
(-) = No response

Note (a) Twenty fifth week of gestation (c) Increasing frequency prior to the twenty fifth week of gestation (d) Increasing frequency following larger than the smaller doses of pituitrin

Table 1 shows the results of the experiment. The first column gives the dose of pituitrin which they exhibited con-  
response frequency following larger than the smaller doses of pituitrin

frequency with which they exhibited contractile responses to pituitrin is shown in Table I, arranged according to the amount of drug administered and the time in gestation at which it was given. It will be observed that the patients who received 3 minims of the drug gave more responses than those who received less. The columns on the right of

Table I also show that the frequency of the responses increased as pregnancy advanced

There appeared to be differences in the incidence of response of various individuals to the drug. Of the 32 patients, 30 gave a response and 2 (patients 4 and 21, Table I) did not, 2 more (patients 3 and 13) gave only 1 response each.

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TABLE II.—TIME BETWEEN TREATMENT AND CONTRACTILE RESPONSE

Weeks of gestation	No. of patients	No. of treatments	Average time—seconds
25	1	1	918
29	1	1	612
30	3	3	414 ± 22
31	4	4	855 ± 187
32	8	8	429 ± 81
33	7	7	370 ± 54
34	9	9	561 ± 40
35	10	10	385 ± 74
36	10	10	415 ± 45
37	11	11	293 ± 43
38	10	10	403 ± 87
39	11	11	260 ± 34
40	8	8	376 ± 40

Average interval in time between treatment and response of patients who received 3 minims of pituitary extract (Table I). Note shortening of interval as pregnancy advances.

The character of the responses was quite uniform; only 1 patient (patient 29) exhibited an atypical response, and this showed a quantitative rather than a qualitative difference. The patients who exhibited typical responses presented the following characteristics:

**Subjective symptoms.** Of the 313 treatments which were given, 68, or 22 per cent, produced either a feeling of tightness—56 treatments—or of actual pain. All of the latter reactions occurred after the thirty-first week of gestation.

**Interval between treatment and objective response.** It is of interest, first, to note that no patient experienced a response prior to the twenty-fifth week of gestation; second, that responses did not necessarily appear each week after they were first observed. The interval between treatment and response bore a direct relation to the duration of gestation. The intervals of the patients who received 3 minims of pituitary extract are shown in Table II, in relation to the duration of pregnancy. The nearer to labor the treatment was given, the shorter was the interval.

**Character of typical contractions produced by pituitrin.** The typical contractile response of

TABLE III.—FREQUENCY OF CONTRACTIONS AFTER ADMINISTRATION OF POSTERIOR PITUITARY EXTRACT

Weeks of gestation	No. of treatments	Average No. of contractions per hour
25	1	21
26	1	25
27	1	18
28	2	12
29	2	25
30	2	17
31	4	20
32	6	27
33	9	24
34	8	19
35	11	16
36	12	22
37	13	19
38	20	17
39	17	16
40	18	16

Showing frequency of contractions after administration of pituitary extract, arranged according to duration of pregnancy. Note slowing of rate as pregnancy advances.

the uterus to pituitrin consisted essentially of a series of clonic contractions. The frequency of these was determined for 136 of 162 treatment periods. The maximum was 37, minimum 3 and the mean  $19 \pm 6.6$ . The mean rate by weeks of gestation is summarized in Table III. It was found to be more variable and higher from the twenty-fifth to the thirty-sixth week than thereafter.

A good example of a typical response to pituitary extract is shown in Figure 2. It will be observed here, that although the contraction waves in general are very much alike, in many instances the first wave fails to disappear completely before the second one begins. This tendency toward a tetanic type of contraction, in connection with the initial part of the response, is very characteristic of the response of the pregnant uterus to pituitrin. The contraction wave resulting from the administration of pituitrin resembles very much the waves which occur spontaneously at different times during pregnancy, but both differ from the waves which occur during the first stage of normal labor. It will be observed



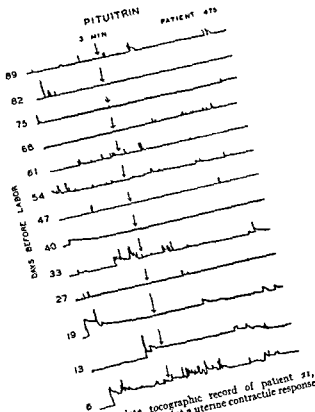


Fig 1 Complete tocographic record of patient 21, Table I, whose uterus failed to exhibit a uterine contractile response to 3 minims of pituitrin at any time

in the records shown in Figure 2, that the contractile phase of the waves following the administration of pituitrin is of short duration and therefore the rising arm of the wave is nearly vertical, whereas the descending arm is less steep. As pregnancy advances the total length of the wave increases but this is largely due to increase in the period of relaxation. During normal labor the rise of the wave is much slower than before labor, or following the administration of pituitrin. This marked difference in the pattern of the contraction following the administration of pituitrin, from that which occurs at the time of normal labor, may help to explain the difficulty encountered in attempting to induce labor by the use of oxytocic drugs.

The typical response and its relation to the tension of the uterine wall. As pregnancy advances the uterus undergoes not only intermittent contractions, but also changes in the

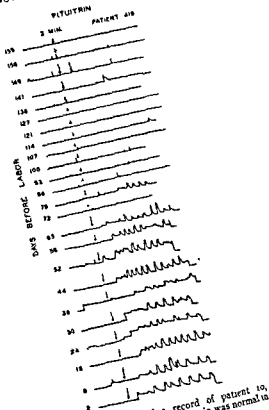


Fig 2 Complete tocographic record of patient 10, Table I, whose uterine response to pituitrin was normal in character

tension of its wall which are independent of its contractions (2). As yet this characteristic of the pregnant uterus has been studied little.

We have been made conscious of these changes in tension because the use of the tocograph makes it possible to distinguish differences in tension which otherwise cannot be detected. The tension can be measured in the following manner. The instrument is placed upon the abdomen. If the uterus is not tense, the recording button sinks into the abdominal wall, and the recording lever continues undisturbed. A tense uterus, on the other hand, will force the button into the machine and raise the recording lever, in proportion to the tenseness of the underlying uterus. The distance traversed by the recording lever when the tocograph is placed upon the patient is a measure of the tenseness of the uterus.



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amount, a typical contractile response will follow the administration of pituitary extract. If the individual produces a subnormal amount, the response to pituitary extract will be either feeble or imperceptible. If she is elaborating too much of the hormone, the tension of her uterus will be unusually high; the administration of pituitrin in such a case will further increase the tension.

If the consideration mentioned has any foundation in fact, then this knowledge will aid in the proper use of pituitrin at the time of labor. It readily explains why certain patients fail to react to pituitrin, why most of them respond normally, and why a few experience tetanic spasms which may cause fetal death, or rupture of the uterus.

Unusual tension of the uterus can be detected by means of the tocograph. When it is found, it is a contraindication to the use of pituitrin. By using this knowledge we may be able largely to avoid the two dangers just mentioned.

## SUMMARY AND CONCLUSIONS

Posterior pituitary extract was administered to 32 women at regular intervals during pregnancy while their uterine contractions were being registered with a Lóránd tocograph. Two patients failed to experience a uterine response to the drug at any time during gestation; 29 experienced a characteristic reaction; and 1 exhibited an unusual response.

Patients who experienced typical responses exhibited the following characteristics: (1) a series of clonic contractions occurring at a rate of approximately 20 per hour; (2) onset of contractions after the twenty-fifth week of

gestation; (3) a wide variation in the time in pregnancy at which they were first observed; (4) inconsistency with respect to appearance of contractions after they were first noted; (5) a shortening of the interval between treatment and onset of uterine response as pregnancy advanced; (6) a slowing of the contraction rate as pregnancy advanced; (7) no unusual tension of the uterine wall before treatment.

An atypical response was observed in a patient possessing an extreme degree of tension of the uterine wall. The pretreatment tension was increased by pituitrin, resulting in a prolonged, intensely painful spasm.

From the above observations the following conclusions are reached:

1. Patients vary widely in their uterine response to pituitrin during pregnancy.
2. The contraction pattern depends largely upon the tension of the uterine wall.
3. An evaluation of the tension of the uterine wall before the administration of pituitrin at the time of labor may assist in the avoidance of accidents which result from prolonged and severe tetanic spasm.

The author is indebted to Dr. Dorothy L. Ashton for the privilege of studying the patients upon her service at the Sheltermg Arms Home.

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# THE BACTERIAL CONTENT OF AIR IN THE OPERATING ROOMS

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UP to the period of about 1865 many people held the view that what we now recognize as infection was a spontaneous process on the part of tissues. The development of minute living forms in dead tissue of plant or animal origin was referred to as spontaneous generation. The belief that certain of these minute forms were related to, if not the cause of, infection stimulated critical minded workers to study the basic problems of fermentation and putrefaction. The demonstration of the minute particles suspended in air as being related to decomposition was one of the contributions by Tyndall, a mathematician and physicist. By means of a crude box, through which a beam of light could be passed, he proved that "spontaneous generation" did not take place when all the particles within had settled out so that the beam of light was no longer visible from the side. At this early date Tyndall was actually using a beam of light to analyze air for the presence or absence of bacteria-laden particles. Stimulated by research on the bacterial nature of fermentation, putrefaction, and infection, Lister conceived the idea of operating upon patients in an atmosphere of a solution of phenol to prevent infection of the wound from the contaminating air particles.

Since that time the development of surface asepsis and antisepsis relative to surgery has occupied the attention of many investigators to such an extent that many other possibilities have been overlooked so that today instruments are scrupulously cleaned and sterilized with heat, the operator is clothed in a sterile uniform, a mask is placed over the nose and mouth with the intent of preventing bacteria therefrom coming in contact with the wound, the patient is carefully draped with sterile linen, so that only the area involved in the operation is left exposed. Antisepsis was developed so that potent germicides are used in the attempt to sterilize or at least disinfect the skin of the patient at the site of operation. In more recent times, many investigators, particularly Meleney (6, 7) and Hart (1, 2, 3, 4), have called the attention of surgeons to the air as a possible source of infection in otherwise "clean" surgical wounds. Meleney (6) reported a 9 year study of operative infections and, after carefully considering the various resources, listed them in order of importance as follows: (a) nose and throat of operators, (b) hands of the operator, (c) skin of the patient, (d) air of the operating room, (e) instruments and materials. By exposing Petri dishes in the operating room he found ten times as many organisms on operative days as on non-operative days. However, no data were presented to substantiate this statement. He emphasized the fact that the study in itself made the staff "infection-conscious" and care of each detail led to a reduction in the incidence of infection. Hart (1), after studying the source of infection in operated wounds, says, "as soon as a Petri dish of blood agar was exposed to the air in the operating room the source of our infections was evident. Invariably large numbers of organisms, predominately staphylococci (albus and aureus), settled out of the air. . . . Cultures from the walls and ceilings showed Staphylococci to be present." He was of the opinion (2) that air conditioning greatly reduced the bacterial content of the air. Later he (3) presented data to demonstrate that the number of pathogenic bacteria in the air of a room increases directly with the number of occupants, although we cannot agree that these data may properly be so interpreted. More recently he (4) has presented data (obtained by exposing one blood agar plate per week for a period of one year) and has inter-

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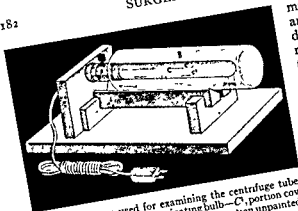


Fig. 1. Device used for examining the centrifuge tube, B, A, electric switch, C, illuminating bulb—C, portion covered with white paint to reduce glare, C', portion unpainted, D, support

interpreted them as demonstrating a relationship between the number of bacteria in the air and the incidence of wound healing. As a result of emphasis on the air as a possible source of infection in the so-called "clean" operative wound, ultra violet lamps are now available to sterilize (?) the air—especially that immediately over the operative field. Recent work by Wells (13), however, suggests that, in such a system, there are inherent defects which definitely limit its usefulness for this purpose.

#### PURPOSE OF THE INVESTIGATION

Because of the occasional infection of "clean" surgical wounds in our local hospitals we undertook to study their possible and probable sources. Since the literature contains so much indirect evidence that such bacteria in the wounds come from the air and thus indirectly from the operating personnel, we felt work along this line should constitute the chief phase of our investigation, at least in the beginning. We, therefore, proposed to study thoroughly the bacterial flora in our own operating rooms, keeping as complete and accurate records as possible concerning various activities in the room during a working day which we considered might influence the bacterial population of the air. In order to have complete, detailed information, it was proposed that chronological records should be kept of the number of people in the room, whether they wore masks; whether the nurses, doctors, or students, when the nurse started preparing for the operation and how

much time it required and whether there was any undue activity in such preparation; the duration and kind of operation and details relative to cleaning the room after the operation. All these factors were then to be considered in connection with the bacteriological data in order to interpret completely the results of each day's experiment. In other words, it was proposed to study first hand and by direct fashion the cause-effect relationship between the number of people and their activity in a room and the bacterial flora of that room. On the basis of such data we would then be in a position to decide in a logical fashion upon the proper method for correcting the procedure and thus minimize the incidence of infections. At the same time additional investigations were started to determine other possible sources of infection besides the air. Data bearing on these will be presented later.

#### METHODS USED

1. The Petri plate method was used throughout the course of the investigation, partly because it is a commonly accepted procedure, and partly to obtain sufficient data to show the errors of such technique. The Petri plates were the standard 100 millimeter diameter were the standard 100 millimeter diameter size, containing blood agar of the following composition: Difco nutrient broth, 2 per cent agar agar, 6 per cent citrated human blood. The plates were incubated aerobically at 37 degrees C for 48 hours and examined on a Quebec colony counter. In order to have fair sampling of the air and at the same time not interfere with the surgical procedures, it was decided to expose routinely four such plates, each time for a period of one hour, a fifth plate being placed on the operating table when it was not otherwise in use. The distribution of the plates is shown in Figure 2. The plan was to expose the plates at various times of the day in such a fashion that the data so obtained might be compared with the data obtained from the Wells' air centrifuge. Sets of plates were therefore exposed (as regularly as possible) from 7 to 8 a.m., 9 to 10 a.m., 10 to 12 a.m., 1 to 2 p.m., and 3 to 4 p.m., thus covering the period of activity in the operating room. (This required the exposure of 20 to 25 plates per day as compared with one per

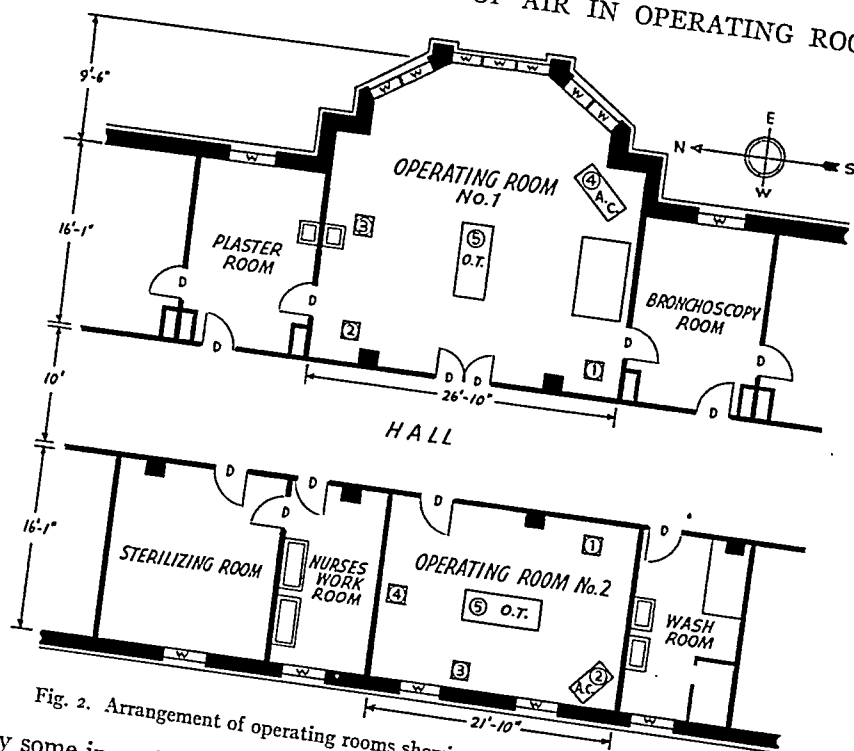


Fig. 2. Arrangement of operating rooms showing distribution of Petri dishes.

day as used by some investigators). Samples were usually collected on alternate days of the week (Monday, Wednesday, and Friday) during the first part of the investigation (November to February), and on Tuesday, Thursday, and Saturday during the remainder of the time. Sunday samples were collected at random throughout the winter and summer months.

2. The Wells' international air centrifuge (11) was used to collect periodic samples at hour intervals throughout the day, usually from 8 a.m. to 4 p.m. On specified occasions samples were collected at half hour intervals. The instrument used was operated to draw 10 cubic feet in 6.5 minutes. Duplicate samples were always collected. The medium used was blood agar, kept fluid in a sterile thermos bottle. Experience soon demonstrated that if the medium was kept longer than approximately 3 hours the blood began to turn brown, making the examination of the tubes difficult because of the opacity. The medium was also unsatisfactory from the point of view of hemolysis (alpha or beta). The tubes were exam-

ined on the illuminating device shown in Figure 1, in which *A* represents the electric switch, *B* the centrifuge tube to be examined, carried on support *D*, *C* the illuminating bulb with portion *C*<sup>1</sup> covered with a white paint to reduce glare and portion *C*<sup>2</sup> left unpainted. The bulb is a 25 watt inside frosted Mazda lamp manufactured by Westinghouse. Dr. Kenneth MacDonald, University of Iowa, suggested the original form, of which this is a modification. Centrifuge samples were collected on the same days the Petri plates were collected. The tubes were incubated 48 hours at 37 degrees C. aerobically. The samples from outside the operating room on the second floor were obtained by suspending the centrifuge on a rope hanging from the third floor window immediately above the operating room and pushing the instrument away from the wall by means of a wooden pole. The samples inside the operating room were taken with the instrument placed on a table 3 feet high, this being not only a convenient height, but also at a level comparable to the Petri plates and to that of the patient on the operating table.

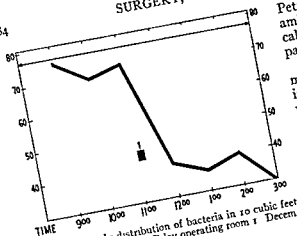


Fig 3. Hourly distribution of bacteria in 10 cubic feet of air, door open all day. Riley operating room. December 4, 1939

The original plan was to collect samples from directly over the operative field by means of a sterile rubber tube (1 inch inside diameter) extending from the patient to the intake of the centrifuge. It should thus be possible to examine the air in the immediate vicinity of the operative field directly in place of indirectly by examining air from other parts of the room. As a preliminary experiment to prove the system would operate, a 10 foot piece of tubing, 1 inch inside diameter, was adapted to the intake of the air centrifuge. The opposite end of the tubing was then placed at different levels of the room and duplicate 10 cubic feet air samples collected. These samples were then compared with the air samples collected without the rubber tubing in place. Only an occasional colony developed in the tubes used to collect air drawn through the rubber tubing, whereas the counts ranged from 65 to 80 in the tubes used to collect samples directly, i.e., without the rubber tubing. The experiment was repeated several times with similar results, indicating that such a procedure could not be used for the proposed experiments in the operating room.

3. Dust analyses were made on a few occasions with the hope of obtaining data which might be correlated with the bacteriological findings. For this purpose the standard impingers for dust analysis were used, with a rate of flow of 1 cubic foot per minute. Samples were collected for periods of 1 hour each at intervals corresponding to the exposure of the

Petri plates. Portions of the samples were examined in the standard counting chamber and calculations made to determine the number of particles per cubic foot of air.<sup>1</sup>

4. Humidity determinations were made by means of the sling psychrometer at hourly intervals to correspond as closely as possible with the rest of the samples collected on those days.

5. Temperature determinations during the winter and spring months were automatically controlled, and since there appeared to be no demonstrable relation between temperature and the bacterial content of the air, such determinations were not continued throughout the full period of investigation.

6. Complete data were recorded concerning the number of people present, the amount and kind of activity in the operating room, whether the windows were open and if so whether there was a demonstrable breeze, and all other minor conditions which might possibly be considered as influencing the bacterial flora.

7. We have tried the apparatus described by Hollander and Dalla Valle, but found it unsatisfactory because we were not able to obtain results which were either uniform or comparable to any other procedure available.

8. Operating room technique: As a general rule, anyone entering the operating room wore a mask over the nose and mouth if an operation was being performed. At all other times no mask regulation was enforced. During warm days in the fall and spring seasons it was not uncommon to have at least one window partially open, even during an operation. In the late spring and summer days the windows were quite uniformly open and at times (especially on uncomfortably hot, humid days) an electric fan placed on the floor was operated to add to the comfort of the operating personnel. During the summer months, as has been the practice in past years, the doors to the operating rooms were commonly, though not always, allowed to remain open during operations.

9. In order that the reader may properly interpret the various problems relative to

<sup>1</sup>The dust analyses and humidity determinations were made by J. F. Keppler and J. S. Wiley under the supervision of Dr. Louis W. Spaulding, director of the Bureau of Industrial Hygiene, Indiana State Board of Health, and we take this opportunity to express our appreciation for such assistance.

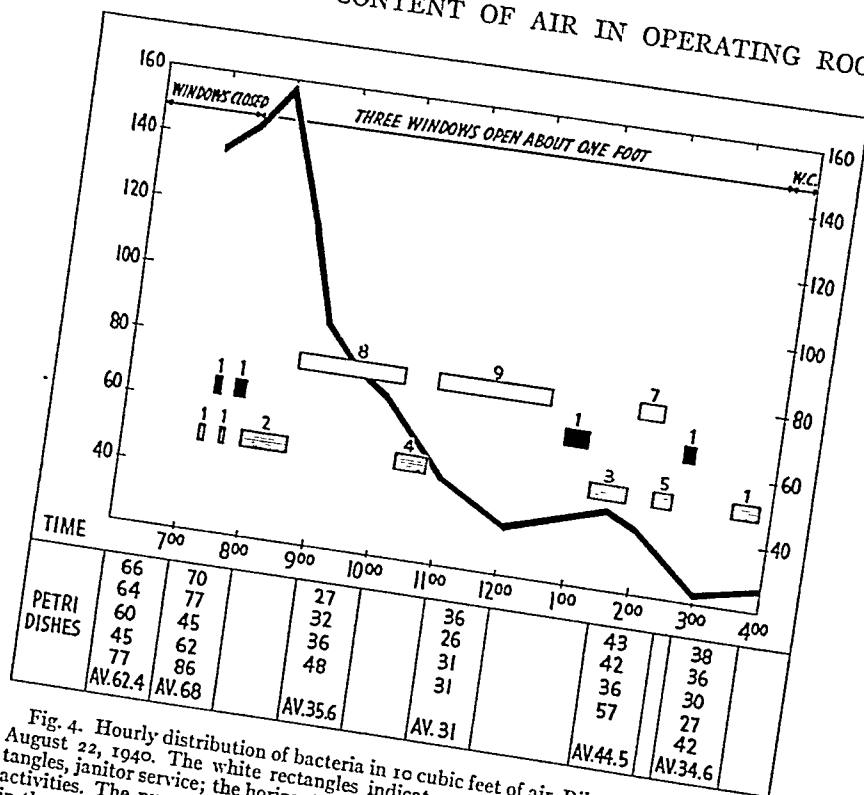


Fig. 4. Hourly distribution of bacteria in 10 cubic feet of air, Riley operating room 1, August 22, 1940. The white rectangles indicate period of operation; the black rectangles, janitor service; the horizontal lined rectangles, preoperative and postoperative activities. The numerals above the rectangular areas indicate the number of people in the room.

#### ANALYSIS OF DATA

In the early part of the investigation, samples of air were collected by the air centrifuge method on the assumption that a direct relationship existed between the number of bacteria laden particles in the air and the number of persons in the operating room. Consequently, most of the samples were obtained during the working day. Analyses of the data as they were accumulated indicated very clearly that the bacterial count was about twice as high in the morning as in the afternoon. This was to be expected since all of the operations had been done in the morning. As there were no operations and data of the type represented in Figure 3 were obtained. Data of this type were obtained on several occasions and it soon became apparent that the general distribution of bacteria in the air of the operating room for any given day varied in

sampling the air, as well as understand the various factors which may influence the experiments, a diagram is presented in Figure 2 to show the size, shape, and relative positions of two of the operating rooms where the major part of the data was obtained. The positions of the exposed Petri dishes are clearly indicated by the encircled arabic numerals. The numbers given correspond to the positions of the data given in Figures 4 to 8 inclusive, the top figure in the chart being represented by the position number 1, the second by number 2, etc. This investigation covered a period of time extending from late November, 1939, to September 13, 1940, during which time the bacterial content of the air in the operating rooms was determined on 85 separate days. The investigation involved the examination of over 1,500 samples taken with the air centrifuge and over 1,800 Petri dishes were exposed.



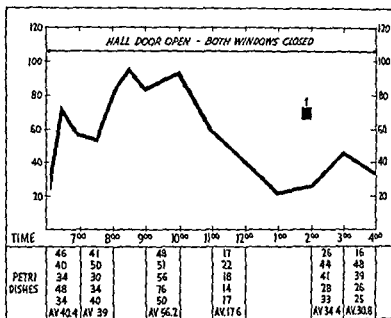


Fig 5 Hourly distribution of bacteria in 10 cubic feet of air, Riley operating room 1, April 16, 1940

this fashion, irrespective of activity, number of persons, or whether operations were performed. Figure 4 shows very clearly that the high count is not dependent upon either number or kind of operations, number of people in a room, or the nature of the activity. During the first operation 8 people were present in the room, during which time the count dropped to about half what it was before the operation. During the second operation the count continued to drop in spite of the presence of 9 people. From the data represented in this particular chart it is impossible to determine whether the high morning count is due to the cleaning and pre-operative activity or to some other factor. The continued low count in the afternoon when pre-operative and postoperative activity is just as great suggests that some other explanation should be sought. In the light of other information now available, it may be that the sudden drop at 9 o'clock is due to the opening of the windows. While the averages of the counts obtained by the Petri dish method follow a general trend simulating the air centrifuge data, examination of the individual counts reveals a marked variation

from hour to hour for a given position and from one position to another for a given hour.

In an attempt to determine the cause of the "high morning-low afternoon" counts data were kept relative to every possible related factor. At first the radiators were considered, the assumption being the early morning heat would set up convection currents and resuspend particles which would slowly settle out for several hours. It was soon discovered that the temperature in the rooms remains constant in the fall, winter, and spring months (when the work was just well started) and convection currents were just as great in the afternoon as in the morning. The effect of the ceiling lights and the operating lamps as possibly influencing the counts was soon ruled out by obtaining similar data on non-operative days when the lights were not being used.

Since operating room 1 is on the east side of the building and has a large bay window, the possibility of the sunlight charging the air particles to keep them in suspension was considered. This was shown not to be the case by obtaining similar data from operating room 2 which is just across the hall from room 1 and

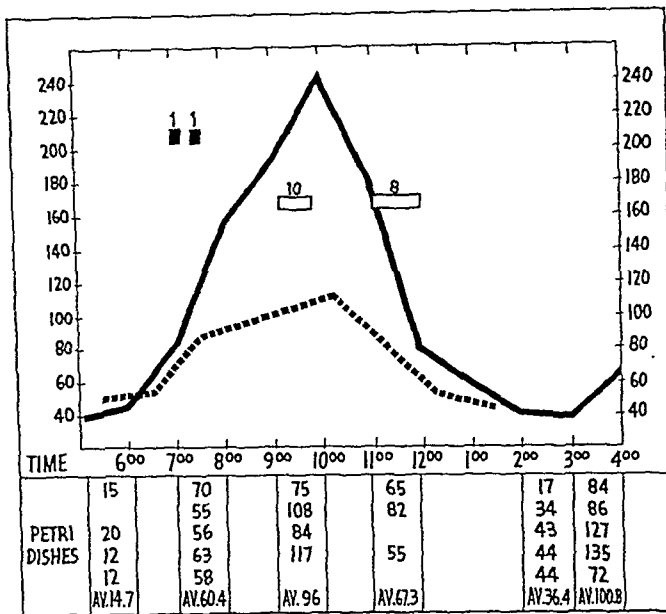


Fig. 6. Hourly distribution of bacteria in 10 cubic feet of air, March 28, 1940, Riley operating room 2, black line; hall outside operating room, interrupted line.

on the west side of the building. If sunlight were related to the phenomenon of "high morning-low afternoon" counts in operating room 1 then the reverse should be the case in operating room 2, i.e., the counts should then show "low morning-high afternoon" distribution. Such was found not to be the case. In bacteriological analysis of the air of 3 operating rooms in 2 buildings on two different levels (second floor and fifth floor) similar hourly distributions have been found to prevail as a general condition, yet one operating room looks north, one east, and one west.

Since smoke investigations revealed air currents entering operating room 2 via the transom, we considered the possibility of dust from the traffic in the hallway as possibly being the source of the organisms. Samples were therefore collected early in the morning and it was soon found (Fig. 5) that the bacterial count is low as late as 6 a.m. and then begins to rise rapidly during the next 2 or 3 hours. Apparently this was the source of the high bacterial count in the morning samples since the activity in the hallway is greatly reduced by approximately 11 a.m. In order

to prove the validity of this hypothesis dust counts were made in the hallway and in the operating room at the same time bacterial samples were collected. The dust counts plotted in millions per cubic foot against time followed the same type of distribution as the bacterial counts shown in Figure 6; i.e., the dust counts were lower in the hallway than in the operating room. While such data are entirely opposite to those expected, we repeated them enough to believe they represented actual existing conditions.

Since data obtained earlier in the summer indicated that the bacterial content of the air in the operating room was lower with the windows open samples were collected outside the windows on certain days to see how they would compare with those taken inside. Since only one air centrifuge was available and since insects came into the room when the screens were removed, only a few days were suitable for collecting such comparable data. An example of such data is shown in Figure 7. This shows the low count in the air 6 feet outside the window on a still day as contrasted with the high count inside the operating room. It

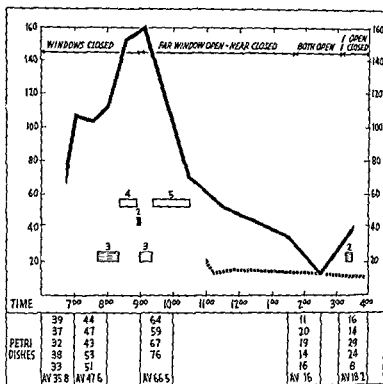


Fig 7 Hourly distribution of bacteria in 10 cubic feet of air, August 20, 1940, in Riley operating room 2, black line, outside window, interrupted line

also shows that during an operation when 5 people are working, with the windows open there was a rapid decrease in the bacterial content. Figure 7 also shows that the early count is lower than "mid-morning" and that the trend is rapidly upward before there is any activity in the room. Figure 4 more graphically demonstrates the effect of opening the windows because in it the rapid decline is noted at 9 a.m. when the tendency normally is to be at a peak whereas in Figure 7 the decline begins about 10:30 which has been found sometimes to occur normally.

It would be erroneous to present data showing only uniformly smooth curves to represent the bacterial population in the air of the operating room. While the data for a given day are usually represented by relatively smooth curves as herewith shown, there were days when the variations were quite marked as shown in Figure 8. There was no known activity within the room or adjoining hallway

or climatic conditions outside (e.g., winds) which could logically account for this fluctuation. Attention is called to the counts on the Petri dishes exposed for the two periods 7:30 to 8:30 and 9:00 to 10:00; there being wide differences within each group exposed at a given time, the two averages, however, being identical but differing greatly from the data obtained by the air centrifuge.

Since it is customary in many hospitals to postpone certain elective major operations until summer, it was of interest to analyze the data on bacterial content of the air in the operating room according to seasons. In order to show the variations it was decided to use months in place of seasons since the latter vary considerably. Probably it would have been better to have used weekly averages but the data available would hardly justify such analysis. An examination of Figure 9 shows very clearly the uniform tendency for the bacterial count to be high during the morning

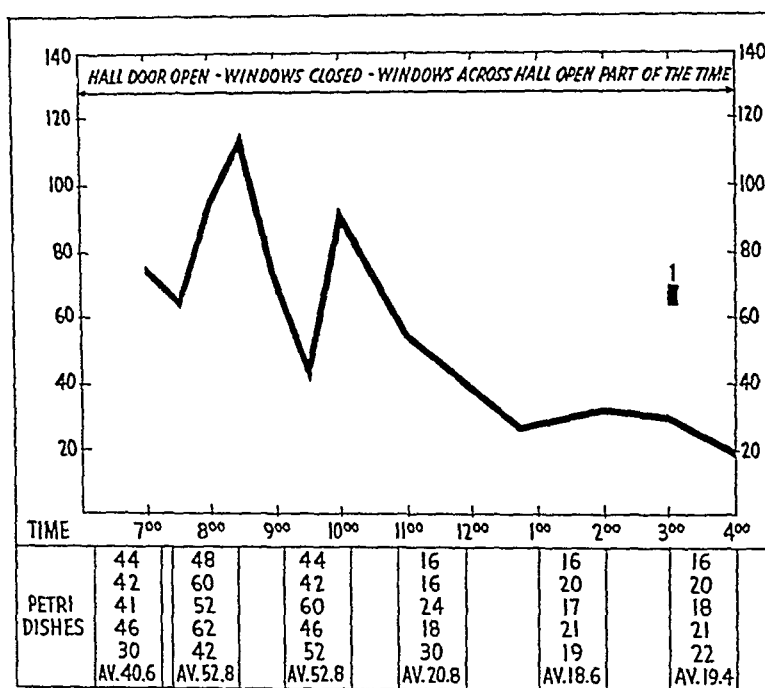


Fig. 8. Hourly distribution of bacteria in 10 cubic feet of air, August 2, 1940, Riley operating room 2.

hours and low in the afternoon, irrespective of the month; one exception being in July when the variations are irregular. Not enough data were available for the month of May to be statistically important although those available follow the same general trend as for April and June. It is significant that from an examination of the data in Figure 9 alone one might justifiably conclude that the high morning counts were due to the increased activity relative to operations performed at that time but it has been demonstrated repeatedly that there is no real cause-effect relationship between such operations and the magnitude of the count. It is emphasized that the data for the averages represented in Figure 9 were obtained under a variety of conditions but which nevertheless represented the type of conditions under which the operations were performed, i.e., windows open and closed, doors open and closed, sometimes with one, few, or several people in the room.

In order to demonstrate the manner in which the count varies from month to month

for a given hour of examination the data were plotted against the months as abscissa as shown in Figure 10.

#### EVALUATION OF STUDY

While we have pointed out that a bacteriological examination of the air by means of exposing Petri dishes is not a reliable procedure, it would still appear that the falling bacteria-laden particles and not the suspended droplet nuclei would be the ones important from the standpoint of infecting exposed wounds. With such variations as we encountered in routine examination, however, it is obvious that the procedure cannot yield reliable data even from the standpoint of wound infections. Had we exposed at the hourly intervals only a single Petri dish as some have done, the results would have varied significantly according to the particular location designated for the exposure. In fact the data by Hart (3) show just such a variation. We can only speculate as to what the data would have shown had we collected air samples with four or five air cen-

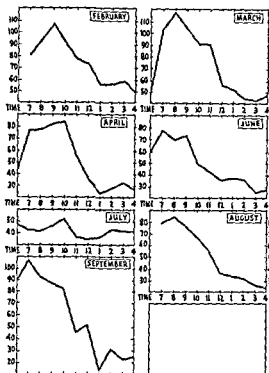


Fig. 9. Average hourly number of colonies from 10 cubic feet of air, during several months in 1940, Riley operating room 2.

trifuges located at the various places in the room corresponding to the exposed Petri plates. Irrespective of the location of exposure, the Petri dish counts tend to be much higher in the morning than in the afternoon. Without further consideration, one would naturally attempt to correlate this with the amount of activity, since nearly all the operations are performed in the morning. However, when one considers all the data for a given day it becomes quite evident that a cause-effect relationship does not exist between the operative procedures and the high bacterial count. While Hart (3) interpreted his data as suggesting such a relationship, we do not feel that they warrant such an interpretation. We recognize the value of statistical analyses but a careful examination of the data obtained for a given day will not allow a deduction that the number of contaminated particles (large enough to fall or small enough to remain suspended) in the air of the operating

room are the result of or proportional to either the number of people or the amount of activity in the room. In this connection we would refer to data obtained on a day when a bilateral radical mastoidectomy was performed between 1:30 and 3:30 in the afternoon. The air samples taken during the operation contained no more organisms than those taken before or after, and less than those taken during the morning.

If the infected particles in the air do not come from the occupants, either directly or indirectly by resuspending dust particles, one must find some other suitable explanation of their presence. We therefore studied the air currents in the operating room by means of smoke and found that while there were no air currents coming in from the windows, there was a marked flow of air into the room from the hallway via the transom. In view of the extensive traffic in the hall we studied the bacterial content of the air in the hallway on the half hour and in the operating room on the hour (Fig. 6). The data obtained show that there are fewer bacteria-laden particles in the hallway than in the operating room for a given period. This is especially significant since patients, nurses, doctors, students, and ward help moved about freely in the hallway without masks. Even in the winter months, contrary to current belief, we found the bacterial content of the air lower in the hallway than in the operating room. However, the count was higher in the morning than in the afternoon, simulating qualitatively the hourly distribution found in the operating room. Correlated with the bacteriological examinations were the dust determinations which showed the same type of hourly distribution but with fewer particles in the hallway. It should be emphasized that the "high morning-low afternoon" counts are obtained at various seasons of the year and on nonoperative days as well as on operative days. Because of the latter we secured the co-operation of the housekeeping department and eliminated all cleaning on certain days, but the general distribution of infected particles remained the same. The production of convection currents from the radiators being heated in the morning was ruled out because the radiators are thermostatically controlled

and the temperature in the fall, winter, and spring months does not vary more than 1 to 2 degrees—day or night. The effect of sunlight on the air was considered as possibly being related to the peculiar distribution, but this hardly seems plausible since the condition existed in each of the three operating rooms; one with a north, one with an east, and the other with a west exposure. Again, contrary to current opinion and what one would ordinarily expect, the "high morning-low afternoon" type of distribution is lost if the windows are open. It is true that the Petri dishes sometimes indicated a high count immediately on opening the windows, probably due to a sudden inrush of air carrying dust from the window sill, but after a few minutes the air flora, as measured by the air centrifuge, dropped markedly and rapidly. This fact suggested that the organisms in the air of the operating room were coming from the occupants, but we believe that the rest of our data not only do not support the idea, but disprove it to a great extent, or, we believe, entirely, since samples collected during the time of operation and while the amount of activity was at its height showed no increase over those taken at other times and samples taken on nonoperative days showed the same general distribution as those taken on operative days. Under these circumstances, if activity in the room increases the bacterial count by the Petri dish method, there should be a similar change in the counts of the air centrifuge method when the counts are taken simultaneously. It further suggests that the air in the operating room should be changed frequently to reduce the number of bacteria in the air. Since one has no control over the outside air it should preferably be filtered to make it free of bacteria, and warmed in the winter months. This is certainly not a new idea, but the basis for the suggestion we believe is new.

If the bacteria in the air are not directly related to the incidence of wound infection the natural question is: What else might be the source of the organisms? The following sources have been mentioned by other investigators: nonsterile gloves, nonsterile operative site, nonsterile equipment (instruments, sutures, ligatures, and drains) and finally, organisms

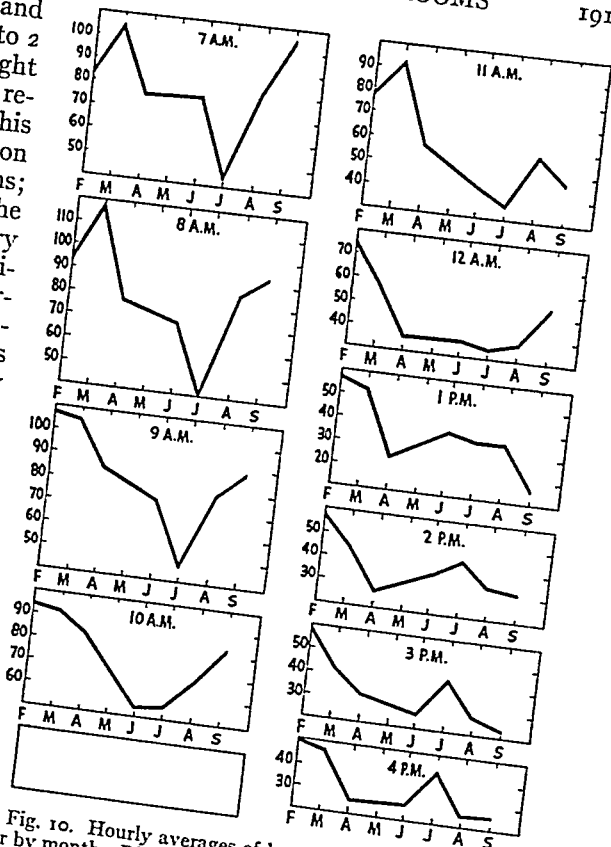


Fig. 10. Hourly averages of bacteria in 10 cubic feet of air by months, Riley operating room 2.

which are present in the patient's own tissues. It is neither logical nor probable that any one factor is all important as a source of infection (unless it be the patient's tissues). It is necessary, however, to investigate all possible sources in order that each one may be properly evaluated. Other phases of the work are in progress and the data obtained to date support the suggestion that a clean wound may be infected by bacteria coming from perforated gloves, nonsterile equipment, and the patient's own tissues.

The elimination of organisms from the nose and throat has been given much consideration in the past and is the basis of the commonly used practice of wearing a mask over the nose and mouth during surgical operations. Recently there have appeared some very graphic demonstrations of the number of bacteria possibly thrown into the atmos-

sphere during coughing, sneezing, and talking (9, 14). To our knowledge, however, there has been no demonstration that bacteria are disseminated into the atmosphere during the process of normal respiration. In fact, our own experience (unpublished) has been that bacteria are not eliminated during either quiet or forced expiration, so long as there are no large droplets of saliva expelled, such as occur with talking, sneezing, and coughing. In support of this idea is the work of Rooks, showing that the nasal passages actually remove large numbers of organisms from the inspired air. Wells (12) has shown that droplets of 0.1 millimeter in diameter or larger fall very rapidly. As far as possible infection of clean surgical wounds in the operating room is concerned, it would appear that these would be much more important than the droplet nuclei. Since apparently no reliable data are available on the efficiency of the various types of commonly used masks, we can only conjecture as to the real surgical importance of bacteria coming from the nose and mouth of the operating personnel. This problem is under investigation at present.

#### SUMMARY AND CONCLUSIONS

1. Data are presented to show the hourly fluctuations in the bacterial content of the air in three separate operating rooms in current use at the Medical Center. The samples were collected from three operating rooms on 85 separate days, and involved over 1,500 determinations with the Wells air centrifuge and exposure of over 1,800 Petri dishes. The period of examination covered winter, spring, and summer months.

2. Irrespective of the season of year, the bacterial content of the air during morning hours (8:00-11:00) was commonly twice that found during the afternoon. Such high morning counts were demonstrated not to result from the amount or kind of activity nor the number of occupants in the operating room. No satisfactory explanation for this type of distribution has been found.

3. The bacterial content of the air was found to be slightly lower during the summer months than during the winter, but only significantly so when the windows were open.

4. The Petri dish method, in our experience, was not a satisfactory method for determining the bacterial content of the air. While there were certain disadvantages in using the Wells air centrifuge for this purpose, we believe it the best method available for large volumes of work.

5. While the bacterial content of the air in the operating room may occasionally be a source of infection for the clean surgical wound, we believe its importance has been greatly overemphasized.

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# THE PROBLEM OF THE TREATMENT OF PERITONITIS

## Preliminary Report

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**P**ERITONITIS is the chief complication that surgeons dread in abdominal surgery. Much experimental work has been done on the production and prevention of peritonitis in animals, with attempts to correlate these findings with the prevention of peritonitis in human beings. The purpose of this paper is to compare the relative efficacy of certain substances in preventing peritonitis in rabbits.

In general, peritoneal protection may be produced by five methods: (1) intraperitoneal use of certain drugs and antiseptics; (2) introduction of a vaccine into the peritoneal cavity, producing a general immunity in which the peritoneum shares—true immune process; (3) antibacterial sera—passive immunity; (4) local protection of the peritoneum attributable to a local hyperleucocytosis and afforded by the intraperitoneal introduction of any number of vaccines and other substances; (5) use of agents, such as deep x-ray therapy.

### INTRAPERITONEAL USE OF CERTAIN DRUGS AND ANTISEPTICS

While certain chemicals may kill organisms *in vitro*, when introduced into the peritoneal cavity, they often cause more irritation than good. Recently the use of sulfanilamide has enjoyed some popularity. Garlock and Seley believe the incidence of peritonitis following operations on the colon to be decreased if sulfanilamide is given for 3 days preceding operation and for several days thereafter. Ladd, Botsford, and Curnen state that the high mortality rate in primary peritonitis in infants and children can be markedly reduced by early operation and drainage followed by adequate treatment with sulfanilamide in the streptococcal group and type-specific serum in the pneumococcal group. Ravdin and his

coworkers found that the mortality in appendicitis with peritonitis was lowered from 1.4 to 0.4 per cent following the use of this drug. Corry, Brewer, and Nicol report similar results in the treatment of peritonitis of appendical origin with sulfanilamide. However, it is unfortunate that peritonitis secondary to appendicitis was used as the test case, as in our experience even in cases of generalized peritonitis of appendical origin, 60 per cent of the cases recover with conservative therapy (Sperling and Myrick).

Our interest in the possible use of sulfanilamide intraperitoneally dates back to 1938, when Jensen and his coworkers found that the incidence of infection in compound fractures was less when sulfanilamide was placed in the débrided wound.

At the University of Minnesota Hospitals, sulfanilamide in divided doses of 4 to 6 grams a day is given subcutaneously in most cases of peritonitis irrespective of its origin. On 3 occasions 10 grams of sulfanilamide were poured into the peritoneal cavity at laparotomy when peritonitis was present. While all the patients were critically ill at the time of operation, the fact that 2 of the patients died made us cautious as to the further use of sulfanilamide intraperitoneally in such doses when peritonitis was already present. At present sulfanilamide in doses of 3 to 4 grams is placed in the peritoneal cavity of selected patients when there has been actual or suspected contamination at operation. The powdered sulfanilamide is dusted around the anastomotic sites (3 to 4 grams) and an additional 2 grams are sprinkled also in between the different layers in closing the abdomen. Varco, in this experimental laboratory, has shown a distinctly lowered mortality rate in dogs following complicated gastrointestinal anastomosis when sulfanilamide was used intraperitoneally (unpublished data). Experi-

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mental work will be presented in this paper which shows that the "preperitonitis" use of sulfanilamide is of some value.

#### THE USE OF INTRAPERITONEAL VACCINATION AND SUBSTANCES TO PRODUCE INTRAPERITONEAL HYPERLEUCOCYTOSIS

In 1894 Issaef introduced the idea of vaccination to prevent postoperative peritonitis. Pierrelini in 1897 found that a leucocytic exudate could be produced by the intraperitoneal injection of saline solution and other inert substances. Garnier demonstrated that bacteria were rapidly destroyed in the presence of a leucocytic exudate in the peritoneal cavity; his studies showed the importance of phagocytosis in protecting the patient from peritonitis. In 1902, Soleri produced a peritoneal leucocytic exudate in animals and found that animals with such an inflammatory reaction of the peritoneum survived a colon bacillus peritonitis.

In 1922, Johnson first used amniotic fluid to prevent postoperative adhesions and later to protect against peritonitis. He explains the action of amniotic fluid on the peritoneum as one that produces a protective layer of fibrin on the serous surfaces and a moderate local leucocytosis which is followed later by a complete resolution of the fibrinous deposit. He describes the peritoneal reaction as a defense response characterized by hyperemia, marked subserous edema, increase in the pink-tinged toneal fluid, and the formation of a pink-tinged fibrinous exudate. There is an increased white cell count that rises rapidly for about 12 hours, at which time the differential count shows a marked preponderance of polymorphonuclear leucocytes. Following this peak, the neutrophils are replaced by histiocytes until the cell count becomes predominately histiocytic. If the exudate is removed from the peritoneal cavity, it forms a fibrinous clot. The peritoneal exudate following intraperitoneal injection of vaccines is profuse and hemorrhagic and does not clot when exposed to air.

Steinberg and Goldblatt began their extensive work on peritonitis in 1926. They showed that intraperitoneal immunization by living and heat-killed colon bacilli produced an immunity in animals to subsequent colon

bacillus and fecal peritonitis. They presented convincing evidence that when colon bacilli in saline suspension were injected intraperitoneally they were rapidly absorbed into the blood and lymph, but such animals practically always survived. However, when equal doses of colon bacillus were suspended in 1 per cent gum tragacanth, the animals did not get a bacteriemia but invariably died. One explanation of this was that toxic products of the bacteria were formed in quantity only when they were retained within the peritoneal cavity, and that these toxic products caused the death of the animal.

David and Sparks in 1927 showed that when colon bacilli were injected intraperitoneally they passed readily into the blood and lymph. However, when a plastic peritonitis was first produced by injection of a turpentine emulsion, organisms subsequently injected intraperitoneally could not be recovered from the blood or thoracic lymph.

Herrmann in 1927 showed that in order to produce a peritoneal exudate in rabbits, it was necessary first to build up an immunity before the infecting material was injected. This was successfully carried out by the use of repeated small intraperitoneal doses of a vaccine prepared from the *Bacillus coli* and *Streptococcus viridans*. At autopsy the animals showed a true fibrinopurulent peritonitis, but control animals receiving no such immunizing vaccine died with no signs of peritonitis.

In 1931, Morton injected various substances into the peritoneum, such as dextrose broth, heated streptococcal filtrate, various solutions of glucose and saline. Using rabbits he found that he was able to establish a certain degree of protection in most of the animals.

Rice, in 1933, attempted to immunize the peritoneum of dogs by the injection intraperitoneally of a mixture of staphylococcus, streptococcus, and *Bacillus coli* bacteriophage filtrates. The animals were given the bacteriophage before or at the time of operation which consisted in tying off the cecum in order to produce peritonitis. Bacteriophage failed to immunize the peritoneum in his experiments; moreover the formation of plastic exudate seemed to be inhibited. Jern, Harvey, and

Meleney, working with mice, reported the effect of bacteriophage on peritonitis due to *Bacillus coli*. They were able to protect the animals against such an infection even when they used doses twenty-five times the size of the lethal doses for controls. The phage was effective when used intraperitoneally before, during, or even several hours after the injection of colon bacilli.

#### BACTERIOLOGY OF PERITONITIS

Roberts, Johnson, and Bruckner maintain that in the vast majority of human cases the peritoneal cavity is not sterile. They obtained positive cultures in 76 per cent of their cases in which the peritoneum was opened in clean operation. However, these organisms were practically the same as those which they obtained from the deep layers of the skin before the peritoneal cavity was opened, which would seem to indicate their source. The organisms were chiefly diphtheroids or staphylococci which were also found in the laboratory air. Rather surprising was their finding that cultures from frank infections of the peritoneal cavity did not yield a very much higher percentage of positive cultures than cultures from the noninflamed cavity.

The colon bacillus seems to be the commonest organism encountered in peritonitis of intestinal origin. In 1891, Malvoz stated that peritonitis of intestinal origin should not be attributed to any bacteria other than the *Bacillus coli*. In 1938 Altemeier reviewed the literature of the bacteriology in perforated appendicitis. Most of the authors quoted by Altemeier believed the *Bacillus coli* to be the commonest organism encountered, although he found the bacterial flora in some cases to be very complicated and bizarre. Owen studied cultures or peritoneal fluids of animals injected intraperitoneally with suspensions of total cecal contents of normal animals, usually the guinea pig. Such cultures revealed members of the coliform group of bacteria in 51 per cent of the cases. Cultures from animals dying of the infection showed the organisms in 84 per cent of the cases while in animals that survived 16 per cent of cases showed these organisms. Streptococci were seldom found and pathogenicity tests gave compara-

tively low death rates. Mixed cultures of streptococci and coliform organisms killed some animals but the streptococci could seldom be found in the peritoneal fluids of animals dead of these injections.

#### CELLULAR EXUDATE IN PERITONITIS

It has been established from animal experiments and clinically in patients that the introduction of foreign substances into the peritoneal cavity will excite the production of a defensive cellular exudate. The contents and volume of this exudate will be determined to a large extent by the character and amount of the substances involved. This reaction is characterized locally by hyperemia, increase in the peritoneal fluid, increase in the histiocytic and leucocytic counts and phagocytosis.

There is no uniformity of opinion as to the relative protective functions of the polymorphonuclear leucocytes and the histiocytes. Steinberg regards the polymorphonuclear as the important phagocytic cell and feels that the histiocyte is a scavenger cell which appears late in peritonitis when it engulfs the degenerated polymorphonuclear leucocytes. Collier and Brinkman also believe that the polymorphonuclear leucocyte is the important cell in phagocytosis. Johnson among others believes that the histiocyte is a superphagocyte and comes into the picture late in response to dead tissue. However, Herrmann expressed his belief that the histiocyte is probably the most important cell concerned with phagocytosis.

Garnier, Wilkie, and Collier and Brinkman found examination of the peritoneal exudate to be of value in determining the progress of acute peritonitis. It should be emphasized, however, that local immunity cannot be measured in terms of one total or differential leucocytic count alone. Other factors, chiefly humoral, play an important part (Johnson, McCollum).

In 1938, Rixford studied at operation the peritoneal fluid of patients who had previously received intraperitoneal vaccine and compared these findings with a control group of patients which had received no vaccine. Specimens were taken with a glass pipette just after the peritoneal cavity was opened. In

unvaccinated cases, the total white cell count averaged from 1900 to 2600 per cubic millimeters of fluid. There were practically no neutrophils, very few eosinophils and basophils, but many lymphocytes and histiocytes—45 per cent. In patients who had been vaccinated 24 to 144 hours prior to operation, specimens of peritoneal fluids were also examined. There was considerable variation in the findings, but it was apparent that there was an early increase in polymorphonuclear cells and a delayed but marked increase in histiocytes.

Seeley, Higgins, and Mann observed the cytological response of the peritoneal fluid of rats to injections of amniotic fluid concentrate, Bagen's vaccine—prepared from colon bacilli and nonhemolytic streptococci—and sodium ricinoleate. They found that with all materials there was an early and rapid rise of polymorphonuclear leucocytes, reaching a maximum in 3 to 6 hours. Histiocytes appeared much later but were the preponderant cells after 6 or 7 days. The response of both cells was greater in those animals receiving sodium ricinoleate.

In 1937, Corwin reported that in the rabbit, the cellular responses to Bagen's vaccine and sodium ricinoleate were nearly identical qualitatively. However, with Bagen's vaccine the cell count of the peritoneal fluid was greatest at 12 hours, with 1 per cent sodium ricinoleate at 24 hours and with 2 per cent sodium ricinoleate at 48 hours. The differential count showed the polymorphonuclear to appear early, being in greatest abundance in 6 to 12 hours, while the histiocytes were maximal in 1 to 3 days. Whereas the cell count per cubic millimeter after injection of sodium ricinoleate was only 40,000, the total amount of fluid was so much greater that a greater total number of cells was evoked by the ricinoleate than by Bagen's vaccine.

Coller and Rife, in their review of the cellular aspect of immunization, state that the variation in opinion regarding the relative phagocytic properties of the neutrophil and histiocyte is due in part to the use of different species of animals by different workers. Also the type of material used, the dosage employed, the time intervals for examination of

the fluids are not constant in the different studies.

#### CLINICAL RESULTS FOLLOWING THE USE OF INTRAPERITONEAL VACCINES AND OTHER SUBSTANCES

Steinberg and Goldblatt developed a protective emulsion consisting of *Escherichia coli* in tragacanth, which they call coli-bactragen.<sup>1</sup> This substance will protect the experimental animal from certain types of subsequently-induced peritonitis. Steinberg has demonstrated protection against living colon bacilli, *Streptococcus fecalis*, *Bacillus pyocyaneus*, and *Clostridium welchii*, in both pure and mixed cultures.

In 1934 Goldblatt reported a collected series of 400 patients receiving coli-bactragen. Eight postoperative deaths were recorded but only 3 of these could be attributed to peritonitis. The operations were performed by various surgeons and consisted chiefly of resections of the large bowel. The first preparation of coli-bactragen was injected intraperitoneally about 24 hours before operation and was frequently accompanied by a rather severe general reaction. The more recent preparations of coli-bactragen produce a less severe general reaction and achieve maximum protection within a few hours.

In 1934, Potter and Coller reported a series of 79 patients, most of whom had major operations performed upon the colon, who were given coli-bactragen before operation. There were 11 deaths, in only one of which was the lethal outcome attributed to peritonitis. Although the series was small and not controlled, they were of the opinion that vaccine was probably not indicated except in cases of gross fecal contamination. In 1936, Coller and Ransom reported the use of coli-bactragen in 79 cases which had a combined abdominoperitoneal resection for carcinoma of the rectum and rectosigmoid. There were 12 deaths, but in none was death believed to be due to peritonitis. In the same year Steinberg reported 391 cases in which coli-bactragen was used before operation or at the time of operation with none developing postoperative peritonitis.

<sup>1</sup>Coli-bactragen (Steinberg) consists of 50 billion bacteria per 30 cubic centimeters with 1 per cent of 1:50,000 mercuriolate suspended in 1:5 per cent gum tragacanth.

In 1928, Barga developed his vaccine prepared from streptococci and colon bacilli. It was given intraperitoneally 3 days before intestinal operations. In 1935 Dixon and Barga reported 1,500 cases in which the vaccine had been used with a reduction of 66 per cent in the mortality rate from postoperative peritonitis. The vaccine was attended with degrees of general systemic reaction. In 1930 Rankin, in a review of 527 surgical lesions of the large intestine and rectum in which peritoneal vaccination was used before operation, reported a mortality rate of 12.3 per cent by patient and 8.6 per cent by operation. In 1933 he reported a new series in which the vaccine was not used. In 200 consecutive operations upon the colon and rectum, he reported a mortality of 5.5 per cent by operation and 8.4 per cent by patient. He attributed the decline in mortality to better preoperative preparation rather than to vaccination.

Johnson, Warren, Trusler, Young and Marks, Klimpton, and others have reported their results with the use of amniotic fluid concentrates. Young and Mark reported upon the use of amniotic fluid concentrates in 49 cases which involved chiefly operations on the colon. There were 3 deaths, but in only 1 inoperative peritonitis. In a series of 46 similar cases in which amniotic fluid was not used before operation, there were 8 deaths, 17.3 per cent. In the cases of colonic reaction the mortality was 38 per cent in the control series. Gelfert believes the postoperative convalescence is smoother in patients receiving amniotic fluid.

#### SERUM

Many clinical studies have appeared in the literature concerning the treatment of peritonitis with various sera. Very little experimental work has been done, however. It is impossible to tabulate or evaluate different series, as the type of serum and method of administration vary widely.

The following antigens have been employed: (1) *Bacillus coli* filtrate; (2) toxins of *Clostridium welchii* or of combined anaerobes; (3) a combination of colon and gas bacillus; (4) enterococci, usually added to colon bacilli and

anaerobes; (5) bacterial bodies as well as colon and gas bacilli; (6) a number of other organisms such as the *Bacillus fusiformis*, *Bacillus funduliformis*, staphylococcus, and intestinal streptococci which have produced a serum to which is added polyvalent antigas-gangrene serum and anticolic serum (Harvey and Meleney).

It should be mentioned that not all the anaerobes found in the exudate in peritonitis are virulent. Also, it is not known that a serum produced against one strain of *Bacillus coli* will be effective against other strains of the same organism. For these reasons, it is doubtful that potent sera can be produced commercially according to our present knowledge.

The first use of *Bacillus coli* serum has been attributed to Guthrie (1915); he used serum together with coli vaccine only in patients who underwent operation and in whom the diagnosis was doubtful. Most of the reports of the clinical use of serum have been in the foreign literature (Vincent, Weinberg, Riemann, Kunz, Pellegrini). In this country Priestley and McCormack reported favorable results in a small group of cases.

One of the best reports is that of Riemann. He reported 368 cases of peritonitis in which either coli serum or a combined "peritonitis serum" was used during the period from 1931 to 1933. He saw no difference in results from the two types of sera. Of 368 cases of peritonitis, 244 followed appendicitis with a 4.5 per cent mortality and 124 followed other lesions with a 20.9 per cent mortality. In previous 3 year periods without the use of serum, the mortality has been from 21.7 per cent to 22.5 per cent for peritonitis following appendicitis and from 37.7 to 38.4 per cent for peritonitis following other causes. Riemann never used over 100 cubic centimeters of serum in treating a case.

On the other hand, Kapel, of Copenhagen, and Urech, of Switzerland, after they had made a fairly extensive clinical trial, found no benefit from serum in cases of peritonitis. Santi had the opportunity to try serum in 14 cases in which for one reason or another an operation was not attempted. Nine of 14 patients died.

Perrando, Chiari and Kunz, Trusler and Moss have reported experimental evidence showing that antiserum gives some protection against peritonitis. However, the series of animals was small and the specificity of the antisera not proved.

#### DEEP X-RAY THERAPY IN THE TREATMENT OF PERITONITIS

For many years, deep x-ray therapy has been used in the treatment of acute and chronic infections. The use of deep x-ray irradiation in the treatment of gas bacillus infections has quite a vogue at the present time. There are occasional case reports concerning the treatment of pneumonia, peritonitis, cellulitis, etc., by irradiation, but most of these are poorly controlled and irradiation was not the only form of therapy used in many instances.

Pratt reported that the preoperative irradiation of the abdomen and pelvis of patients with carcinoma of the colon reduces the incidence of peritonitis. Kelly and Dowell advise irradiation of the abdomen in some patients with peritonitis due to rupture of the appendix. Altemeier and Jones believe roentgen therapy to be of value in immunizing animals against peritonitis. The maximum degree of immunity in animals occurred from 4 to 6 weeks after irradiation. As Blalock remarks, it is too early to appraise the value of this type of therapy at the present time.

Desjardins, from clinical observations and an extensive review of the experimental and clinical reports on the treatment of inflammations with x-rays, suggests that the leucocytes undergo lysis when irradiated, and in this lytic process antibodies are freed in the infected area. Kelly agrees with this idea. Experiments concerning the use of deep x-ray therapy in the treatment of peritonitis in rabbits will be discussed later.

#### EXPERIMENTAL DATA—GENERAL CONSIDERATIONS

The ideal activator of peritoneal immunity is a substance which clinical analysis and extensive clinical and laboratory trial has proved to be innocuous, one which may be used before or at operation without discomfort or

clinical upset; one which has an immunizing interval sufficiently brief to be adaptable to operative introduction; one which will induce a peritoneal reaction similar to that laid down by the normal peritoneum in the presence of infection. In addition, the agent should be stable and free from remote untoward reaction (Johnson and coworkers).

A number of substances has been used to try to prevent peritonitis. As early as 1885, an attempt was made to immunize the peritoneum by colon bacillus vaccine (Mikulicz) but because of the severe reactions that occurred, it was largely given up. Later peritoneal immunization was reported following the use of nonspecific substances, as peptone broth, saline, sterile water, serum, egg albumin, dextrose, and certain drugs and chemicals. Of late years, the following substances have enjoyed a certain popularity: antiperitonitis vaccine (Bargen, Rankin, Dixon), coli-bactragen (Steinberg), coli antiserum (Trusler and Moss), sodium ricinoleate (Seeley and Larson), and sulfanilamide.

It is difficult to evaluate the efficacy of these various agents in preventing peritonitis in clinical cases because factors, as the type of case, the drug and dosages used, time interval, etc., vary so widely. Moreover, it is not justifiable to use critically sick people as controls.

In all immunological studies it is important to realize that all immunity is relative in both a qualitative and quantitative sense; that is, if the dose or virulence of the organism is greater than the protective titre of the substance to be tested, the animal will die. Therefore, experimentally, unless quantitative as well as qualitative factors are controlled, the results are relatively meaningless.

*Method* The peritoneal exudate from patients dying of peritonitis was chiefly used. This material was collected and the organisms examined as to number and identity. Several loopfuls of the material were inoculated into liver peptone broth. After 24 hours of incubation, a smear was made and stained by Gram's method. A loopful of the liver peptone culture was streaked upon blood agar and cosin-methylene blue plates for identification of organisms. Another loopful was inoculated into a tube of sterile milk and incubated at

37 degrees C. for 6 to 24 hours for determination of anaerobes.

To count the number of bacteria, the culture was drawn up to a mark on a capillary pipette; blood was drawn up to the same mark and the contents of the pipette blown out on a slide and mixed. A smear was made and stained by Wright's method. The number of bacteria and red cells in 100 fields were counted and averaged. The number of bacteria were calculated by proportion.

$$\frac{\text{Average number of bacteria per field} \times \text{erythrocyte count per c. mm.}}{\text{Average number of red blood cells per field}} = \text{No. of bacteria per c. cm.}$$

Full grown, stock rabbits were used as the experimental animal. In each case the culture used was 24 hours old. In a few experiments the rabbit was anesthetized with drop ether, the abdomen was opened under sterile precautions, and the culture was placed in the peritoneal cavity followed by the drug to be tested. In most of the experiments, however, the culture was injected into the peritoneal cavity of unanesthetized rabbits followed after a few minutes' interval by an injection of the drug through the same needle. Control experiments were carried out. The animals were observed up to a period of 2 weeks following injection.

The survival rate was studied as well as the incidence of peritonitis, as the animals that survived the 2 week period were not sacrificed to see if they had peritonitis. Animals that died within 24 hours after injection of the culture showed little evidence of peritonitis and probably died of a bacteremia.

The following substances were tested: sodium ricinoleate 1 per cent as prepared by Dr. W. Larson, department of bacteriology, University of Minnesota Medical School; ether U.S.P.; tincture of merthiolate; mercurchrome, 2 per cent (aqua); S. T. 37; hydrochloric acid, 0.5 per cent; hydrochloric acid, 1 per cent; cow serum; coli-bactragen (Steinberg); immune rabbit serum from 2 sources; fanilamide. Bovine serum was tried because of its well known resistance to peritonitis. Immune rabbit serum was obtained as follows: A cardiac puncture was performed on rabbits that survived 10 to 14 days following the in-

jection of a peritoneal exudate. After the clotted blood was centrifuged, the agglutination titer of the pooled serum against *Escherichia coli* was determined. This serum was injected intravenously into other rabbits to note its protective power against peritonitis. This is, in essence, an immunotransfusion. "Hyperimmune" serum was made from blood of rabbits that survived 5 injections 2.5 cubic centimeters each, of a purulent peritoneal exudate given over a period of 2 weeks. This exudate contained *Escherichia coli* and *Streptococcus viridans*, 250,000,000 organisms per cubic centimeter.

## RESULTS

*Experiment 1.* Culture: 2 cubic centimeters of brain broth of a peritoneal exudate containing *Streptococcus viridans*; *Staphylococcus aureus*, aerogenes; unidentified gram negative and positive rods and cocci; and *Escherichia coli*.

No quantitative study of the organisms was made. The rabbits were anesthetized with ether, and the abdomen was opened under sterile precautions. Two cubic centimeters of the culture was added and then 5 cubic centimeters of the drug to be tested.

### EXPERIMENT I

Drug	No. of animals	Dead			Living		
		No.	Duration days	Peritonitis	No.	Duration days	Peritonitis
Controls	8	6	1	6	2	14	2
Sodium ricinoleate, 1%	8	1	2	1	7	14	1
Ether	8	2	3	2	6	14	1
Tincture merthiolate	8	2	1.1	2	6	14	4
S. T. 37	8	3	1.4	3	5	14	3
Mercurchrome, 2%	8	4	1.3	4	4	10	4
Hydrochloric acid 0.5%	8	2	1.4	2	6	10	6*
Hydrochloric acid 1%	8	2	1.2	3	6	10	3*

\*Bowel locally was burned by acid with scattered splattered areas.

In this experiment, sodium ricinoleate 1 per cent, ether, and tincture of merthiolate were the most effective drugs in preventing peritonitis.

*Experiment 2.* Culture: 2 cubic centimeters of veal broth containing *Streptococcus viridans*, *Escherichia coli*, and *Clostridium welchii*, a total of 500,000,000 organisms per cubic centimeter.

The rabbits were injected intraperitoneally with 2 cubic centimeters of culture followed by 5 cubic centimeters of drug, through the same needle.

## EXPERIMENT 2

Drug	No of animals	Dead			Living		
		No	Duration hours	Peritonitis	No	Duration days	Peritonitis
Controls	5	5	24	2			
Sodium ricinoleate, 1%	5	4	24	1	1	10	
Ether	5	4	24	2	1	10	
Tincture of methiohale	5	5	24	2			

This culture was too virulent. The animals probably died of bacteriemia.

*Experiment 1* Culture 1 cubic centimeters of veal broth containing *Escherichia coli* and *Streptococcus viridans*, a total of 250,000,000 organisms per cubic centimeter

The culture was injected into rabbits intraperitoneally, followed by injection of 5 cubic centimeters of the drug through the same needle

## EXPERIMENT 3

Drug	No of animals	Dead			Living		
		No	Duration hours	Peritonitis	No	Duration days	Peritonitis
Controls	5	2	24		5	5	2
Sodium ricinoleate, 1%	5	0	24		5	5	2
Ether	5	4	24	3	1	3	
Tincture methiohale	5	3	24		2	3	2

With a less virulent culture the longest survival rate was in animals injected with sodium ricinoleate 1 per cent.

*Experiment 4* Culture 5 cubic centimeters of cecal content of rabbit was added to 10 cubic centimeters of tap water

Under ether anesthesia to sterile precautions, the abdomen of the rabbit was opened and 5 cubic centimeters of suspension was added and then 5 cubic centimeters of the drug to be tested

## EXPERIMENT 4A

Drug	No of animals	Dead			Living		
		No	Duration days	Peritonitis	No	Duration days	Peritonitis
Controls	5	3	72	2	2	10	2
Sodium ricinoleate 1%	5	1	72	1	4	10	0
Ether	5	3	2	2	2	10	0
Tincture methiohale	5	2	2	2	3	10	1

## EXPERIMENT 4B

Drug	No of animals	Dead			Living		
		No	Duration days	Peritonitis	No	Duration days	Peritonitis
Control	5	4	3	4	1	7	0
Sodium ricinoleate, 1%	3	0	0	0	3	7	2
Ether	5	3	1	1	2	7	0
Tincture methiohale	3	2	2	2	1	7	2

*Experiment 4B.* Culture. Same as in experiment 4A

The rabbits were injected with 5 cubic centimeters of the culture intraperitoneally, followed by 5 cubic centimeters of the drug to be tested, through same needle

In experiments 4A and 4B, sodium ricinoleate, 1 per cent, also proved to be the most effective drug in the prevention of peritonitis in rabbits.

*Experiment 5A.* Culture: Stool of patient with chronic ulcerative colitis, containing *Streptococcus viridans* and *Escherichia coli*, unidentified gram positive and negative rods and cocci, 2,000,000,000 organisms per cubic centimeter

The rabbits were infected with 2.5 cubic centimeters of fecal material intraperitoneally, which injection was followed by 3 cubic centimeters of the agent to be tested

## EXPERIMENT 5A

Drug	No of animals	Living	Dead
Controls	5	2	3
Bovine serum	4	4	0
Coli bacitragin	5	3	2
Amniotic fluid (Ph. Lilly)	6	2	4

*Experiment 5B* Culture Same as in experiment 5A

The same technique was used as in experiment 5A except that 5 cubic centimeters of the drug to be tested was used

## EXPERIMENT 5B

Drug	No of animals	Living	Dead
Controls	8	0	8
Bovine serum	8	1	7
Coli bacitragin	8	3	5
Amniotic fluid (Ph. Lilly)	6	1	5

## SUMMARY OF EXPERIMENTS 5A AND 5B

Drug	No. of animals	Living	Dead
Controls	13	2	11
Bovine serum	12	5	7
Coli-bactragen	13	6	7
Amniotic fluid (Eli Lilly)	12	5	7

Coli-bactragen and amniotin were effective in only about half of the cases and were only slightly more effective than bovine serum.

*Experiment 6.* Peritoneal fluid of a patient dying from peritonitis, containing *Streptococcus viridans* and aerogenes, and *Escherichia coli*, 2,900,000,000 organisms per cubic centimeter. The specific gravity of the peritoneal exudate was 1.042.

Two and one-half cubic centimeters of the peritoneal exudate was injected intraperitoneally into rabbit followed by the drug to be tested.

## EXPERIMENT 6

Drug	No. of animals	Living	Dead
Controls	8	0	8
5 c.cm. sodium ricinoleate, 1%	8	3	5
10 c.cm. sodium ricinoleate, 1%	8	5	3
10 c.cm. cow serum	8	4	4
10 c.cm. coli-bactragen	8	3	5

Sodium ricinoleate, 1 per cent, was more effective in 10 cubic centimeters than in 5 cubic centimeters dose and was more effective than bovine or coli-bactragen.

*Experiment 7.* Culture was same as that used in experiment 6, except it was incubated 48 hours at 37 degrees. It contained *Streptococcus viridans* and *Escherichia coli*, 2 billion organisms per cubic centimeter.

The method was the same as that used in experiment 6.

## EXPERIMENT 7

Drug	No. of animals	Living	Dead
Controls	5	4	1
5 c.cm. immune serum	8	5	3
10 c.cm. sodium ricinoleate, 1%	7	4	3
10 c.cm. coli-bactragen	8	3	5

The animals treated with 5 cubic centimeters of immune serum injected intravenously seemed to be protected as well if not

better than those that received sodium ricinoleate, 1 per cent, or coli-bactragen.

*Experiment 8.* Culture: Peritoneal exudate from a case of fatal peritonitis. It contained *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus hemolyticus*, 2,400,000,000 organisms per cubic centimeter.

Five cubic centimeters of peritoneal exudate was injected intraperitoneally into rabbits with 5 cubic centimeters of immune rabbit serum intravenously at the same time. In other rabbits immune serum had been injected subcutaneously 7 days before the intraperitoneal injection of 5 cubic centimeters of peritoneal exudate.

## EXPERIMENT 8

Drug	No. of animals	Living	Dead
Controls	6	2	4
5 c.cm. immune serum intravenously	8	4	4
5 c.cm. immune serum (injected subcutaneously 7 days before experiment)	8	2	6

"Immune" serum seems to be of value in protecting rabbits against peritonitis; it must be given intravenously. The subcutaneous injection of the serum 7 days before the experiment was of little value.

*Experiment 9.* Culture: Pus from infected wound 3 weeks after appendectomy; contained *Escherichia coli*, nonhemolytic streptococci, unidentified gram positive and negative rods and cocci, 2 billion organisms per cubic centimeter.

Blood from this patient was taken, allowed to clot, centrifuged. Agglutination titer 1:1280 for *Escherichia coli*. This immune serum was injected intravenously into rabbits. Also these animals were given intraperitoneally 2.5 cubic centimeters of the above culture which was incubated in veal broth, each cubic centimeter containing 250,000,000 organisms.

## EXPERIMENT 9

Drug	No. of animals	Living	Dead
Controls	6	2	4
5 c.cm. human "immune" serum	7	5	2

The human "immune" serum in this case, when injected intravenously into rabbits receiving the above culture intraperitoneally gave definite protection against peritonitis. While there may have been antibodies against other organisms in the serum, only the ag-



glutinins for *Escherichia coli* were determined, as it was the predominant organism.

**Experiment 10** The purpose of this experiment was to note the effect of serum which had a low agglutination titer in protecting against peritonitis.

Culture: Exudate from a fatal case of peritonitis containing *Escherichia coli*, *Streptococcus viridans*, unidentified gram positive and negative rods and cocci, contained 29,000,000,000 organisms per cubic centimeter.

Blood was taken from patient with carcinoma of the cecum with fistulous formation. Culture from the fistulous tract was sterile. Agglutination titer blood was negative for *Escherichia coli*.

#### EXPERIMENT 10

Drug	No. of animals	Living	Dead
Controls	5	2	3
5 c cm human "immune" serum	4	1	3

This serum with no agglutinins for *Escherichia coli* gave no protection against peritonitis.

**Experiment 11** Culture: Peritoneal exudate containing *Escherichia coli*, *Streptococcus viridans*, 2,900,000,000 organisms per cubic centimeter.

Rabbits were injected with 2.5 cubic centimeters exudate intraperitoneally and 5 cubic centimeters of hyperimmune rabbit serum intravenously. Agglutination titer 1:6400 for *Escherichia coli*.

#### EXPERIMENT 11

Drug	No. of animals	Living	Dead
Controls	8	1	7
5 c cm hyperimmune serum (1:6400)	8	6	2

Hyperimmune rabbit serum (agglutination titer 1:5120 against *Escherichia coli*) gave definite protection against peritonitis.

**Experiment 12** Culture the same was used as in experiment 11.

The method used was the same as that in experiment 11, except that hyperimmune rabbit serum (agglutination titer 1:1280) was used.

#### EXPERIMENT 12

Drug	No. of animals	Living	Dead
Control	8	2	6
5 c cm hyperimmune rabbit serum (agglutination titer 1:1280 <i>Escherichia coli</i> )	8	7	1

Hyperimmune rabbit serum with an agglutination titer of 1:1280 against *Escherichia*

*coli* gave definite protection against peritonitis.

**Experiment 13.** Culture: Intestinal content of dog with low ileal obstruction. Contained *Staphylococcus aureus* 2,400,000,000 per cubic centimeter, *Streptococcus hemolyticus* 250,000,000 per cubic centimeter, *Clostridium welchii*, and *Escherichia coli* each 500,000,000 per cubic centimeter.

Under ether anesthesia the abdomen of the rabbit was opened and 1 to 5 cubic centimeters of obstructed ileal content was poured into it, followed by 5 cubic centimeters of sodium ricinoleate 1 per cent or 1 gram sulfanilamide. Eight animals were used in each series.

#### EXPERIMENT 13

Culture	Controls		Sodium ricinoleate, 1%		Sulfanilamide	
	Living	Dead	Living	Dead	Living	Dead
5 c cm obstructed ileum content	0	8	3	5	2	6
1 c cm obstructed ileum content	0	8	3	5	0	8
1 c cm obstructed ileum content	2	6	2	5	4	4
1 c cm obstructed ileum content	1	7	4	5	2	5

With this culture, sodium ricinoleate, 1 per cent, was more effective than sulfanilamide in protecting the rabbits, but sodium ricinoleate, 1 per cent was effective in only 40 per cent of the cases.

**Experiment 14** Culture: Peritoneal exudate from a fatal case of peritonitis contained *Escherichia coli* at least 2,000,000,000 organisms per cubic centimeter, *Streptococcus hemolyticus* 1,000,000,000 organisms, *Staphylococcus albus*, gram negative and positive rods and cocci, aerogenes, and unidentified gas formers.

Three cubic centimeters of exudate was injected into the peritoneal cavity of rabbits followed by 3 cubic centimeters of the substance to be tested. When sulfanilamide was tested, 10 grams of powder was suspended in 30 cubic centimeters of tap water, and 3 cubic centimeters of the thoroughly stirred mixture injected through a No. 15 needle into the peritoneal cavity of the rabbit.

#### EXPERIMENT 14

Drug	No. of animals	Living	Dead
Controls	10	2	8
Sulfanilamide (1 gm)	10	5	5
<i>Coli</i> bacteria 3 c cm	10	4	6
Sodium ricinoleate 1%, 5 c cm	10	4	6

In this experiment, sulfanilamide proved to be the most effective agent. Coli-bactragen and sodium ricinoleate, 1 per cent, were equally effective in preventing peritonitis.

*Experiment 15.* Culture: Same as in experiment 14.

(a) Under ether anesthesia, the abdomen of the rabbit was opened and 5 cubic centimeters of the culture added followed by 1 gram of powdered sulfanilamide in the peritoneal cavity. (b) Under ether anesthesia, 1 gram of sulfanilamide was placed under the skin on the back. Five cubic centimeters of above culture was injected peritoneally. (c) Rabbits were given 20 cubic centimeters of 0.8 per cent sulfanilamide solution (80 mgm.) subcutaneously every day for 5 days and then 5 cubic centimeters of above culture was injected intraperitoneally.

#### EXPERIMENT 15

Method	No. of animals	Living	Dead
5 c.cm. culture plus 1 gm. sulfanilamide intraperitoneally	8	7	1
5 c.cm. culture intraperitoneally plus 1 gm. sulfanilamide subcutaneously	4	0	4
5 c.cm. culture intraperitoneally plus 20 c.cm. 0.8 per cent sulfanilamide subcutaneously daily for 5 days (total 0.8 gms.)	8	5	3
Controls	6	1	5

Sulfanilamide placed intraperitoneally at the same time as the culture gave excellent protection against death from peritonitis. Placing the sulfanilamide subcutaneously at the same time as the culture was injected intraperitoneally gave no protection. However, giving the sulfanilamide subcutaneously daily for 5 days before injecting the culture intraperitoneally gave some protection but not as much as that following placing the sulfanilamide in the abdomen.

*Experiment 16.* Culture: Peritoneal exudate of patient dying from peritonitis, containing *Streptococcus viridans* and *aerogenes*, *Escherichia coli* and *Streptococcus hemolyticus*, 2,500,000,000 per cubic centimeter.

Five cubic centimeters was injected intraperitoneally into rabbits. Within 24 hours 5 rabbits so treated were anesthetized and the abdomen was opened. Peritonitis was present in all. One gram of sulfanilamide was sprinkled into the peritoneal cavity. None of the animals survived more than 48 hours.

While the ether anesthesia may have contributed to the deaths of the animals, sul-

famylamide intraperitoneally was of little or no value in treating the peritonitis once it was well established. This experiment has also been tried in 8 guinea pigs with peritonitis. No protection from the intraperitoneal use of sulfanilamide has resulted once the peritonitis is well established.

*Experiment 17.* (a) Effect of irradiation on the cell count of peritoneal fluid.

Three rabbits were treated by means of x-ray therapy to the abdomen. The method was as follows: 250 roentgens were given to the anterior abdominal wall, 220 kilovolts, 60 centimeter distance with 1 aluminum filter.

Three days later, the abdomen of three of the rabbits was opened and the cellular content of the peritoneal fluid was studied. There were only an occasional histiocyte and leucocyte found, and total counts were no greater than those of 3 control rabbits (500 to 1800 cells per c.cm.). The animals were not studied for longer periods because the efficacy of irradiation therapy should be apparent within the first few days after the peritonitis has developed, if the protection is on the basis of hyperleucocytosis.

(b) Because deep x-ray therapy may give a protection other than cellular to the peritoneum against invading organisms, the following experiments were carried out. (1) 5 c.cm. of peritoneal exudate was injected into the abdomens of unanesthetized rabbits. The rabbits were then given deep x-ray therapy to the abdomen by the method described. (2) Culture contained *Escherichia coli* 2,500,000,000 per cubic centimeter. *Streptococcus hemolyticus* 500,000,000 per cubic centimeter, *aerogenes*, *Staphylococcus albus*.

#### EXPERIMENT 17

	No. of animals	Living	Dead
Controls	6	2	4
Deep x-ray	6	1	5

Dr. Carl Lind, Walter Reed Hospital, Washington, and Dr. Clarence Truog, Miami, Florida, who were then in the department of radiotherapy, aided in this experiment.

In this small series, irradiation was of little value in protecting the animals against peritonitis. In another series, 4 rabbits that were ill with peritonitis, all died in spite of irradiation therapy.

*Experiment 18.* Culture: Peritoneal exudate from a fatal case of peritonitis, containing *Staphylococcus aureus*, *Streptococcus viridans*, *Escherichia coli*, and unidentified gram positive and negative rods and cocci, 2,500,000,000 organisms per cubic centimeter.

Five cubic centimeters of culture was placed in the peritoneal cavity of anesthetized rabbits and 1 gram of sulfathiazole powdered in

#### EXPERIMENT 18

Drug	No. of animals	Living	Dead
Control	8	2	6
Sulfanilamide	10	4	6
Sulfathiazole	10	5	5

Sulfathiazole and sulfanilamide were about equally effective in protecting the animals in this series

#### SUMMARY AND ANALYSIS OF EXPERIMENTAL DATA

It is apparent that there is no cure-all for peritonitis. At best, only about half the animals could be protected regardless of the agent tested. Of the substances used in this study, amfetin and coli-bactragen were no more effective than sodium ricinoleate, 1 per cent, as far as the survival rates were concerned. The results obtained with the sulfonamides were impressive, but it may be questioned if the results obtained were significantly better than those obtained with sodium ricinoleate, coli-bactragen, etc.

Sulfanilamide would seem to be most effective in the preperitonitis stage. Once peritonitis has developed, its efficacy is much reduced. Moreover, the direct application of sulfanilamide would seem to be more effective than the subcutaneous administration of the drug or the placing of an equivalent amount of the powder under the skin.

At this clinic sulfanilamide in doses of 3 grams has been placed in the peritoneal cavity at operation when there was suspected or actual contamination. If frank purulent peritonitis is present, sulfanilamide is not only of little value because it will be inactivated by the protein of the exudate, but it is contraindicated as it may aggravate a hepatitis already caused by the peritoneal infection. Clinically sulfathiazole may prove to be more effective than sulfanilamide in the treatment of peritonitis, as the former is less toxic to the liver.

In "clean" cases, there is no indication for the use or any of these agents. In clean incision of the skin in dogs, sulfanilamide af-

fords no higher incidence of healing by primary intention (Jensen and Rea, unpublished data).

In "dirty" or grossly infected wounds, sulfanilamide is valueless, unless a thorough débridement or cleansing of the wound is performed first. Jensen, Nelson, and Johnsrud found that sulfanilamide was most effective in compound fractures before there was any sign of gross infection. Moreover, in infected compound fractures, if sulfanilamide were placed in the wound before débridement or a thorough cleansing, no benefit was obtained. Similarly, in peritonitis, sulfanilamide is most effective in the preperitonitis stage. When peritonitis is present, its value is questionable.

In the few experiments performed, and in the dosage used, radiation therapy gave little or no protection against peritonitis in rabbits.

The use of hyperimmune serum would seem to be of value in preventing peritonitis in rabbits. A feasible plan for its use in human cases has not been worked out as yet.

#### CONCLUSIONS

1 In reviewing the literature, many agents have been used in treating peritonitis.

2 Clinically it is difficult to judge the value of certain substances in preventing peritonitis, as factors such as the amount and type of contamination at operation, organisms present, type of operative procedure performed, the experience of the surgeon, the condition of the patient, etc., have to be considered.

3 In experimental peritonitis, unless qualitative and quantitative factors, such as the number and type of organisms present, are controlled, the results are meaningless.

4 In these experiments, the effect of certain substances in preventing peritonitis in rabbits was studied, controlling the number and type of organisms injected to cause the peritonitis. Unfortunately the same culture could not be used in all the experiments. Of the substances tested, however, none was effective in more than 50 per cent of cases. Sodium ricinoleate, coli-bactragen and the sulfonamides were most effective of the substances tested. It may be questioned if sulfanilamide is superior to the other substances tested in preventing peritonitis.

5. Regarding the use of sulfanilamide in the peritoneal cavity: (a) it is not indicated in clean cases; (b) it is most effective in the pre-peritonitis stage; (c) it is more effective if placed in the peritoneal cavity than if placed under the skin; (d) it is of relatively little value in cases of frank purulent peritonitis.

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# DERMOVASCULAR EFFECTS OF ESTROGEN IN WOMEN WITH MENOPAUSAL FLUSHES

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IT has been observed recently that estrogen has a vasodilating effect upon the smallest blood vessels of the skin,—a dermovascular action. This has been seen directly in the ear of the rabbit (3), and attested indirectly in this species by noting a 13 per cent reduction in transmitted light following injection of the hormone (2). In the human male, a similar effect has been noted; estrogen causes a 46 per cent increase, on the average, in the size of the finger (4). This is confined to the smallest blood vessels beyond the arterioles, as shown by reasons which will be enumerated.

The present experiments on women in the menopause were carried out as a counterpart to the earlier ones in the male. Particular point is given these newer observations, however, inasmuch as there is as yet no precise information concerning the nature of the mechanism by which estrogen contributes to the relief of vasomotor flushes of the climacteric. The hypothesis that it is concerned in some way with depression of an overactive pituitary gland (1) leaves unanswered the question of how this, in turn, affects the vasomotor system, on one hand, and there is evidence, on the other, to show that an overactive anterior hypophysis is not necessarily manifested by disturbances of the vasomotor system (3). It appeared likely, therefore, that some clue concerning the therapeutic efficacy of estrogen in the menopause might come from a study of the peripheral vascular action of estrogen in carefully selected patients. The following account records the first of our observations along these lines.

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## PATIENTS AND PROCEDURES

Twenty-four patients were directed to us from a large number attending the Outpatient Clinic of the Greenpoint Hospital. The only complaint in these cases was that of intense and frequent flushes from which the patients sought relief. After careful examination, it was established that the individuals were free of other important medical complications. Even so, it was found subsequently that 6 were unsuited to or unco-operative for the purposes of this work, and so were not employed. Of the remainder, 13 were in artificial menopause, 4 were in natural menopause, and 1 was still menstruating.

As a result of intensive observation, it was learned early in the course of study that these patients could be divided into 2 groups. One—3 in surgical menopause, 4 in natural menopause—was promptly relieved of the vascular disturbances by means of estrogenic hormone, there appeared to be no other important contributing factor to the etiology of the menopause syndrome than that of primary ovarian deficiency. The other group—8 in surgical menopause, 2 in irradiation menopause, and 1 still menstruating with premenstrual tension and menometrorrhagia—obtained little relief with estrogen or sedatives, but they responded well, for the most part, to correction of a psychogenic factor. In the account which follows (Table I), it was found desirable to consider the response of the blood vessels in the finger to estrogen on the basis of these two groups. This was so since certain differences were found to characterize the dermovascular action of estrogen in each group.

The management of the patients was systematic. They were given estrogen twice weekly for the first 2 to 4 weeks, until some improvement in vasomotor symptoms was noted. When some relief was obtained, the injection interval was increased to a week. With continued subsidence of symptoms, it was lengthened to 10 days, then to 2 weeks. From this time on, the injection interval was increased as the condition of the patient permitted. The results, from the standpoint of symptomatic relief, have been summarized in detail elsewhere (5) and so will not be reviewed here. In some cases, measurement of the dermovascular effects of estrogen could not easily be made, owing to extreme nervousness of the

<sup>1</sup>The hormones used in this work were generously supplied by various concerns as follows: Abbott, estrone, estrin, Ciba, estradiol, estradiol-dipropionate and testosterone propionate; Parke Davis & Co, estrone, Schering Corporation, estradiol and estradiol benzoate.

patient, especially at the outset of the treatment. In other cases, no attempt was made to record the response with each injection, but only at intervals of 4 to 6 weeks. Records were made during somewhat more than half of the estrogen injections. The technique of recording finger volume changes was exactly that employed by us before (5). The patient was comfortably seated in a room which was free from noticeable drafts. An arm rested on a pad just below the level of the heart, and a finger was inserted into a small glass finger plethysmograph. The only change from our previous procedures was that in this work the movements of the recording droplet were made on moving photographic paper. In the work on human males, readings were made of the position of the droplet in the pipette leading from the plethysmograph, and the curve of finger volume constructed from these readings. After a suitable initial control period in which the position of the droplet remained unchanged, injection of estrogen was made subcutaneously in the opposite arm or intramuscularly in the gluteal muscle. Upon completion of the injection, the light beam to the camera was interrupted, and the record thus marked. Minute intervals were recorded on the paper automatically by means of a suitable timing device. The records were continued for a half hour period, during which time the initial vascular action, if any, of estrogen may be observed. The character of the responses observed in these patients is noted below.

### RESULTS

*Types of dermovascular response to estrogen.* In Table I, it will be seen that any of three effects of estrogen on finger volume may be observed in menopausal women. They are, namely, a *flush type*, a *plateau type*, and a *negative* or undiscernible effect of the hormone. The last is self-explanatory. The plateau type of response is characterized, as in earlier work (5), by an increase in finger volume, commencing within a few minutes after injection of estrogen and progressing steadily to a maximum in the course of 20 to 30 minutes. During this time, there is no discernible elevation of skin temperature, as measured by a sensitive thermocouple (No. 30 gauge wire) and a Leeds & Northrop skin-temperature potentiometer. The flush type of response is superimposed upon a plateau response, and is marked by a sudden acceleration in the rate of finger volume increase, and by a measurable elevation of skin temperature of which the subject is aware. This is sometimes accompanied by sweating but seldom by a chill. The flush subsides after a period of 3 to 15 minutes.

TABLE I.—FINGER VOLUME CHANGES AFTER INJECTION OF ESTROGEN IN MENOPAUSAL WOMEN. RECORDED BY MEANS OF A PLETHYSMOGRAPH.

Types of menopause	Condition of patient	Number of observations	Volume change:	
			Before relief	After relief of symptoms
a. Psycho-genic D.T.		(total)	%	%
D.M.	S	8		1.83
V.I.	S	18	1.82	1.36
C.O.	S	12		1.36
J.N.	S	18	1.75	1.62
E.M.	S	12	0.66	0.66
E.M.	S	22	2.00	2.00
M.D.	S	18	2.85	
R.W.	X-ray	12	3.63	1.25
E.P.	S	2		
M.diL.	X-ray	2		
F.B.	M	4	2.54	
	Average		2.18	1.38
b. Non-psy-chogenic				
S.L.	N	11	1.60	1.00
F.W.	S	12		1.38
A.N.	S	17	2.11	2.55
M.M.	N	9	3.66	2.22
H.K.	N	11	2.74	2.00
H.F.	S	10	2.15	0.92
	Average		2.04	1.68

S—surgical menopause

N—natural menopause

M—menstruating

The functional components in the two types of response are clear, partly on the basis of our past work (5) and partly on the basis of principles in physiology which are well established. The plateau type of response, noted in the earlier work (5), was held to be the result of vasodilatation beyond the arterioles. This conclusion stems first, from the fact that the vasodilatation is unaccompanied by any perceptible elevation of skin temperature (i.e., there is no significant increase in the rate of blood flow in the skin); second, from the fact that in the ear of the rabbit, the vessels which dilate under the action of estrogen are seen to be the smallest ones; and third, from the fact that under favorable circumstances, this vasodilatation in the ear of the

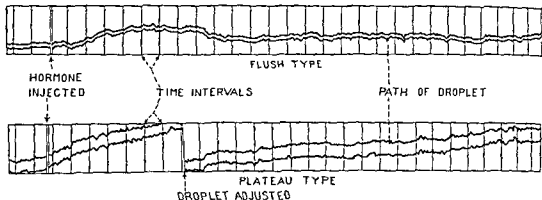


Fig 1. Tracings which were made from continuous photographic records of flush type responses of the blood vessels in the finger to injection of estrogen (top tracing) and of the plateau type of response (bottom tracing).

Plethysmographic records. The first is the result of a period of arteriolar dilatation superimposed upon a background of capillary dilatation. The plateau type is the result of capillary dilatation alone.

rabbit occurs at the same time that a decrease in skin temperature (i.e., arteriolar constriction resulting in diminished blood flow) takes place. Finally, recent plethysmographic measurements by Abramson and co-workers (personal communication) confirm the vasodilatation following injection of estrogen without concomitant increase in the rate of blood flow.

The flush type of response stands in marked contrast to the plateau type just described. In it, the vasodilatation is associated with increased skin temperature. This signifies a local increase in the rate of blood flow—an effect which can be accomplished most readily and most probably by arteriolar dilatation. Such a mechanism involves intermediation of central autonomic connections. This contrasts with the plateau type response which involves capillary blood vessels whose functional capabilities are not demonstrably altered by denervation (3). Such a difference between the 2 types of response constitutes, therefore, a significant point of contrast, and it enables one to draw certain inferences concerning the genesis of the menopausal flush on one hand, and of the mode of action of estrogen upon them, on the other. This is suggested by the incidence of the several types of dermvascular response seen during the course of treatment of the patients listed in Table I.

*Frequency of the 3 types of responses.* A glance at Figure 2 shows that the frequency of the flush, plateau, and negative responses

varies according to, (a) the clinical condition of the patient, and (b) the presence or absence of neuroses as contributing factors to the menopause syndrome. This is exemplified by the following relationships.

Before clinical relief from the vasomotor disturbances of the menopause, flush type responses predominated. They occurred in 68 per cent of the responses seen in the group of neurotic patients, and in 40 per cent of those without a well defined neurosis. Negative responses were virtually nil. After clinical relief, however, plateau responses predominated and negative effects of estrogen were observed much more frequently. Both of these increases were at the expense of the flush type response, seen before there was clinical relief.

On the whole, therefore, clinical relief, whether afforded by hormone, suggestion, or other medication, brings about a decrease in vasomotor instability and in the responsiveness of the smallest blood vessels of the skin to the action of estrogen. The former is, of course, a well known fact among clinicians, but the latter effect has not been known. This decrease in responsiveness of the smallest vessels is attested further by the change in amplitude of the dermvascular response to estrogen, as shown below.

*Quantitative aspect of the dermvascular responses.* In Table I, the average percentage increases in volume of the finger after clinical

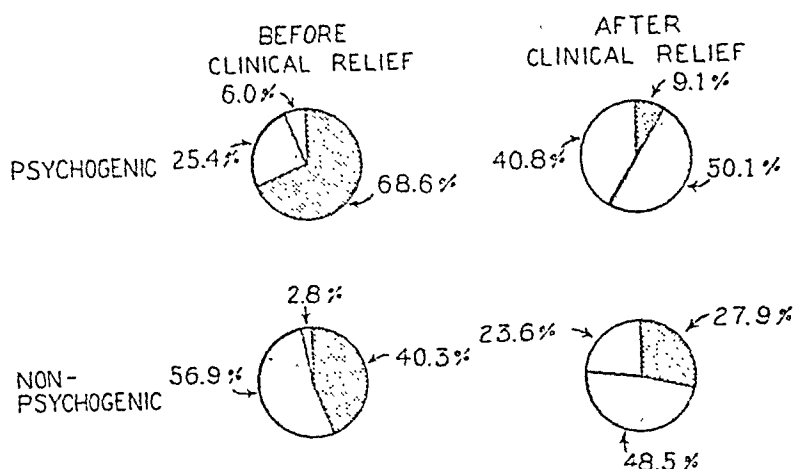


Fig. 2. Diagrams showing the incidence of flush responses, plateau responses, and of negative effects of estrogen on finger volume before, left, and after, right, clinical relief from the vasomotor disturbances of the menopause. At the top, data from women in whom psychogenic factors were largely responsible for the menopausal disturbances; at the bottom, from women in whom no important psychogenic factors were found. Cross hatch, flush response; vertical lines, plateau response; white area, negative.

relief are noted. These are based upon the plateau and negative responses only. Omission of the flush type response seems permissible since it consists of a different physiological mechanism involving arterioles and capillaries instead of capillary blood vessels alone.

It will be seen in the data summarized in Table I that both groups of patients showed,

on the average, smaller responses to estrogen after there was clinical relief than before. The basis for this must be determined by further investigation.

*Sex differences in the dermovascular action of estrogen.* There are two outstanding differences between men and women in their respective dermovascular responses to estrogen.

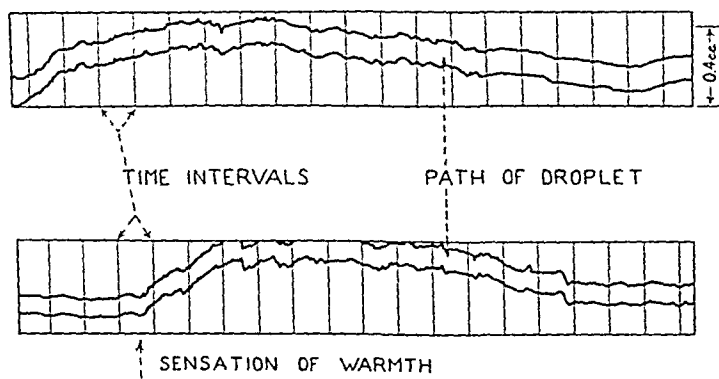


Fig. 3. Two examples of finger volume changes in spontaneous menopausal flushes, uncomplicated by estrogen. The one above lasted about 15 minutes, the one below largely subsided in 11 minutes. The sensation of warmth and suffocation is most noticeable during the rising phase, especially in the type of response in which the initial rise is very rapid. Sweating, when it occurs, is most obvious when the flush is at a peak. In neither of these flushes was there a sensation of chilliness; this follows with more rapid recovery, i.e., vasoconstriction, from the flush.



One is the amplitude of the response, the other, the types of responses seen in the two sexes. In men, the average increase in finger volume was 4.6 per cent, in women, after clinical relief, 1.5 per cent, although negative responses comprised a considerable proportion of the responses.

A more striking difference between men and women, however, was the fact that in no male was a flush type of response observed, whereas it was seen, even after clinical relief, in women. It is possible, of course, that an age difference between the two sexes may account for the variations noted, since the men, for the most part, were in the third decade of life whereas all but two of the women were in the fourth and fifth decades. The two exceptions were 26 and 27 years old. The women, moreover, clearly suffered from a well defined endocrine dyscrasia which the men did not. Consequently, a sex difference in the dermo-vascular action of estrogen is suggested, rather than demonstrated, by these experiments. As they stand, however, the data clearly show that in the 2 groups of men and women with whom we have worked, the capillary blood vessels in men are more sensitive to the action of estrogen than are those of menopausal women who have experienced clinical relief from their symptoms. The reasons for, and significance of, these facts remains to be established.

*The menopausal flush versus the dermo-vascular flush with estrogen.* The question arises of the relationship between the flush type of response which we have frequently observed and the natural flush of the menopause, uncomplicated by estrogen. Records have been made during several such flushes, examples of which are shown in Figure 3. It will be seen from these that the menopausal flush resembles qualitatively that of the estrogen induced flush shown in Figure 1. It rises quickly to a maximum, it subsides quickly, and it lasts for a period of 10 to 15 minutes. The last feature of the flush is interesting inasmuch as the patient notices, —and minds,—the flush in the early, rising phase. This is a period of rapid rise in skin temperature. At the height of the flush, sweating may occur, and this in turn may be followed by a sensation of cold-

ness. When this is marked, decrease in finger volume, i.e., vasoconstriction, takes place more rapidly.

The chief difference between the natural flush and the estrogen induced flush is that the latter is slower to develop and subside. Correlated with this is the more intense sensation in the natural than in the estrogen induced flush. This difference may be explained most readily by the fact that the more rapid the rate of inflow of warm blood into the skin, the more rapid will be the rate of stimulation of the warm receptors in the affected area, and, consequently, the more intense will be the sensation of heat and suffocation.

All in all, therefore, the difference between the natural and the estrogen induced flush appears to be one of degree. The basic physiological mechanism of each is heightened sensitivity of centers in the nervous system to otherwise inadequate stimuli. The relative abatement of the flush type of response to estrogen with clinical improvement, and the absence of flush type responses to estrogen in the group of normal males that we have studied (4), both testify to the correctness of this conclusion. It follows accordingly that the essential physiological disturbance in the menopausal flush involves a primary endocrine dyscrasia coupled with psychic or somatic factors playing upon the peripheral vascular tree, affecting the innervation of the smaller arterioles of the skin on one hand, and the irritability of the contractile elements of the blood capillaries themselves, on the other. Other contributing factors, if such may be involved, remain to be established.

#### SUMMARY

1. There are two different dermo-vascular effects of estrogen observed in menopausal women. These are measurable by means of a finger plethysmograph. They are: (a) A slow, progressive increase in the size of the finger, commencing immediately after intramuscular injection of the estrogen. This is called a plateau response. (2) While a plateau response is developing, a sharp increase in finger volume may occur which reaches a maximum level where it is sustained for 3 to 15 minutes, and then subsides appreciably to

a point somewhat above the preinjection level. This has been called a flush type of dermovascular response.

2. There are two important differences between plateau and flush type responses. With regard to skin temperature, no change is observed in the plateau response, whereas there is an elevation of temperature in the flush type response. There is no significant change, therefore, in blood flow in the former response, whereas there is in the latter. With regard to sensation, there is none definitely associated with the plateau response. With the flush type of response there is a feeling of warmth during the initial phase of the flush, as warm blood apparently rushes into the skin. In this, therefore, there is arteriolar dilatation, whereas the plateau response involves blood vessels lying beyond the arterioles.

3. The relative frequency of these responses in menopausal women is affected by the clinical condition of the patient at the time of injection. Before relief, the flush type of response predominates; after clinical relief, the flush type response diminishes in frequency, and the plateau response increases somewhat. In a significant number of instances, no dermovascular action of estrogen is demonstrable.

4. These changes in the relative frequency of the dermovascular responses were most marked in women whose menopausal condition was relieved through removal of a complicating neurosis, and least marked in those

women in whom no psychogenic factor was discovered.

5. The results recorded may be regarded as objective evidence of increased stability of the vasomotor nervous centers (by diminished number of the flush, or arteriolar dilatation responses), and of the capillary blood vessels (by increased frequency of injections which are not followed by definite dermovascular effects).

6. It is concluded that clinical improvement in the vascular disturbances of the menopause brings about certain adjustments of a stabilizing nature on the peripheral vascular tree, affecting both the arterioles of the skin, and the capillary blood vessels. The extent of this relief is more marked when a complicating neurosis (psychogenic factor) that may be present is removed, and less marked when the menopause is primarily somatogenic in origin.

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## DIVERTICULAR INGUINAL HERNIA

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**L**ITTLE is found in the literature concerning diverticular inguinal hernia. Our attention was first directed to diverticula as an entity by Andrews and Bissell in 1934. Since that time we have kept constant vigil for this type of hernia, carefully recording the operative findings in 2,302 primary hernial repairs performed from January 1, 1935, to June 1, 1940. During the hernia operations, the sac with its attendant accessory locules has been dissected from adjacent structures of the floor of the canal, identified, mobilized, and the relative merit of the muscular and fascial tissues as a stratum determined. Notations were made of the type of diverticulum—whether communicating, noncommunicating, or fatty—and its relation to the direct or indirect sac, the fascia transversalis and the inguinal ligament.

A review of the literature on herniology indicates a lack of fulness of understanding in regard to the inguinal diverticular locule. Diverticula, either because of their rarity or failure of recognition by the general surgeon, have not received the attention they deserve. This conclusion is supported by data submitted in this report and by an analysis of 130 recurrent hernias made by one of us (C. C. B.).

Our purposes in this paper are to determine the incidence of diverticular hernias in a representative series of primary hernias, their type, the relationship to the coexisting sac, and the follow-up statistics, including the percentage of recurrence in 62 primary and 33 recurrent hernias with diverticular locules. Moreover, it is proposed that if this characteristic hernial outpouching or variant occurs with sufficient frequency and plays a rôle important enough, consideration should be given it in regard to its classification as a type of hernia.

Perhaps the incidence of diverticular hernia in this series is high. This may be attributed to (a) the age group with which we are dealing, namely fifth and sixth decades, this age represents the period of beginning decline

with diminution of muscle tone, fatty degeneration, and increased tissue friability, the fascia developing a propensity toward the formation of rents; (b) a more thorough mobilization of all locules of the sac; and (c) our enthusiasm or hernia-mindedness. Since the incidence of diverticula was 13.8 per cent in a series of 130 recurrent hernias, ranking third in the type of sac found, speculation was aroused as to the frequency of diverticula in primary hernias. In searching the literature for the answer, we failed to find any reports on this particular type of hernia save that of Andrews and Bissell, and therefore decided to analyze our own series. It is hoped that others will do likewise and by the accumulation of statistical data, we may be able to arrive at a more accurate incidence.

Possibly some members of our profession may wonder why it is necessary to go into the dissection of these seemingly insignificant hernial locules or variants of the major sac so minutely beyond any apparent practical importance they may have, thus making a relatively simple procedure more complicated and confusing without achieving any notable results other than the removal of these secondary outpouchings and the more elaborate repair. Carefully compiled follow-up statistics show an incidence of recurrence of from 5 to 10 per cent in primary indirect hernias, and from 10 to 20 per cent in direct hernias. In the case of recurrent or secondary hernias, the percentage of recurrence is even higher. It should be noted that the lower figures, as a rule, were obtained in instances of inadequate follow-up. Any surgeon with the impression that his results are superior will become mellowed by a careful survey of his cases carried as long as 5 years. The introductory statement by Seelig, in one of his articles published more than a decade ago, "The modern operation for the cure of inguinal hernia is not as satisfactory as we have grown accustomed to believe," is no less true today. Page, of London, re-examined 206 patients, whose average age

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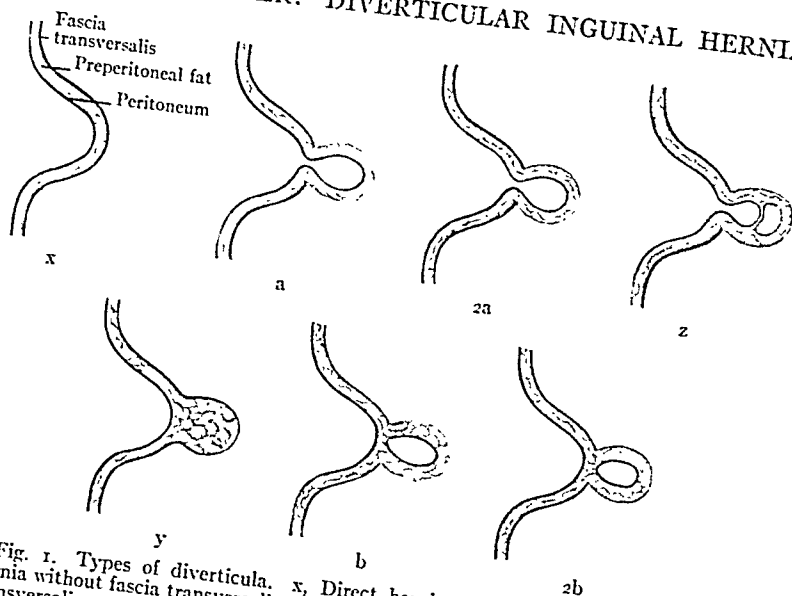


Fig. 1. Types of diverticula. x, Direct hernia; a, communicating diverticular hernia without fascia transversalis; 2a, communicating diverticular hernia with fascia transversalis; z, multilocular diverticular hernia with communicating and noncommunicating locule; y, fatty diverticulum; b, noncommunicating diverticular hernia without fascia transversalis; 2b, noncommunicating diverticular hernia with fascia transversalis.

was 31, from 5 to 9 years after operation. The recurrence rate for indirect hernia was 20.29 per cent and for direct hernia 25.2 per cent. Andrews and Bissell, in their collective analysis of 13 authors, found an average recurrence rate of 20 per cent for direct hernias. These published reports reflect the work of our most experienced and trustworthy surgeons, employing various types of hernioplasties most of which have been in use a decade or longer. Therefore, it would seem that the consensus of most herniologists points to a high incidence of recurrence of inguinal hernia, more particularly the direct type which is usually repaired by the ordinary hernioplastic procedure. This is indicated by every report in which the ultimate results are meticulously scrutinized. Under these circumstances, the most minute anomaly or variant of the sac or wall of the inguinal region may be an important factor in recurrence and is worthy of our ingenuity and best efforts to the end that a more substantial repair may be attained. Up to the present in this era of hernia repair has been the emphasis on the mobilization and exclusive utilization of the all important fascial wall. As expected, with continued progress

there have been modifications in the technique but in the main, these modifications have not deviated from the fundamental principles for the achievement of fascial apposition laid down by Gallie and LeMesurier, Koontz, Wangenstein, McArthur, Zimmerman, and many others.

In contrast with the wall, the sac in recent years has not received comparable attention. In detailing the summary of our findings in regard to the morphology of the sac, frequently we were unable to classify the type of sac at hand. It was noted that the conventional classification had been applicable to hernias that had developed to some size, rather than to those noted in their incipency.

Parsons, in 1937, referred to the indirect-direct type of sac, thus initiating a trend toward classification of inguinal hernia from the standpoint of the position and location of the locule or locules. This seemed to us more accurate and therefore gave impetus to more careful saccular as well as mural dissections. Burton and Ramos used locular division of the sac in their analysis of 130 recurrent hernias. We propose to continue the use of the sac locule as the basis for classification of inguinal

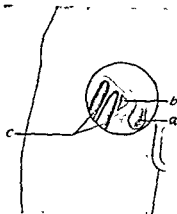


Fig. 2. *a*, Unusual type of diverticular locule emerging beneath the inguinal ligament between the femoral canal and spine of the pubis, *b*, femoral canal, *c*, femoral vessels

hernia: (1) monolocular, which may be either indirect or direct, but preponderantly the former; (2) bilocular, or combined indirect-direct which is more prone to occur in those of the fifth and sixth decades; (3) trilocular, or indirect-direct-femoral, more likely to develop where there is marked structural weakness (these are usually huge and recurrent); (4) sliding, which is unilocular, but so unlike any other type that it would be more confusing to change its present identity; (5) diverticular hernia

#### DEFINITION

A diverticular hernia is a small, pear or sausage-shaped protrusion of peritoneum, or occasionally, fat, coming through a rent in the fascia transversalis. At times the margins of the rent are quite clearly demarcated. Occasionally a funnel-shaped protrusion is formed, presumably due to adherent, attenuated fascia, forming one of the sac coverings. The varying thickness of the coverings and the appearance of the rent have given credence to the theory that the fascia does not bear a constant relationship to the hernia. These endothelium-lined outpouchings of peritoneum are, as a rule, empty, with the exception of the rare fatty ones, which are made up exclusively of smoothly rounded, firm lobules of fat, with very thin connective tissue capsules. The diverticula are usually of uniform size, 3 to 4 centimeters long with a fundus measur-

ing 2 centimeters in diameter and neck approximating 1 to 1.5 centimeters. They arise most commonly as off-shoots from the direct sac or direct locule of the bilocular sac (87 per cent), and usually from the inferior and mesial aspect of its dome, although they may occur independently (Fig. 3).

#### ETIOLOGY

The exact cause of these diverticula, as in the case of diverticula elsewhere, is not known. The existing difference of opinion in regard to the origin of these divers outpouchings attests to their confused etiological status. Many theories have been advanced for the origin of bladder, intestinal and other diverticula concerning which mention has been made of congenital, traumatic, and acquired sources. Muscular and fascial weaknesses subjected to strain, and the effect of normal processes on tissues which have developed abnormal characteristics have also been considered etiological factors. Since there is no vestigial remnant in the inguinal region which might explain their source, one must look elsewhere. The congenital source of hernia is well recognized. The absence of perisaccular and peridiverticular adhesions would tend to eliminate traction as a cause of diverticular development. By exclusion, then, one may regard increased pressure from within as the precipitating factor in the causation of diverticular hernia. In other words, the traumatic pulsion theory is proposed

#### CLASSIFICATION

Diverticular hernia may be of 3 types: communicating (Fig. 1, *a*), noncommunicating (Fig. 1, *b*), and fatty or adipose (Fig. 1, *y*). In our series of 62 diverticular hernias, there were 38 communicating, 21 noncommunicating, and 3 fatty

The communicating diverticulum consists of a direct extension of the peritoneum through a small, constricted aperture in the posterior wall of the canal, with a narrow isthmus or stalk, perhaps not any larger than the diameter of a lead pencil leading into the bulb like fundus. Sometimes the tip of the finger can be inserted into the locule from within the abdomen, which facilitates its dissection from

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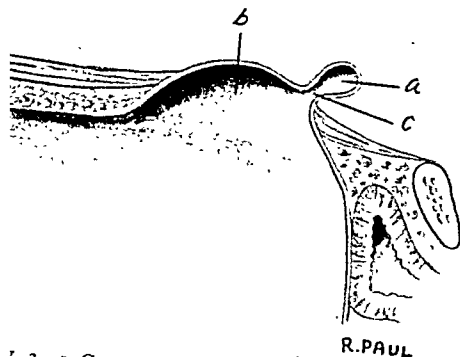


Fig. 3. *a*, Communicating diverticular hernia springing from the dome of a direct sac; *b*, direct sac; *c*, note the narrow neck of the diverticular locule contrasted with the wide neck of the direct sac.

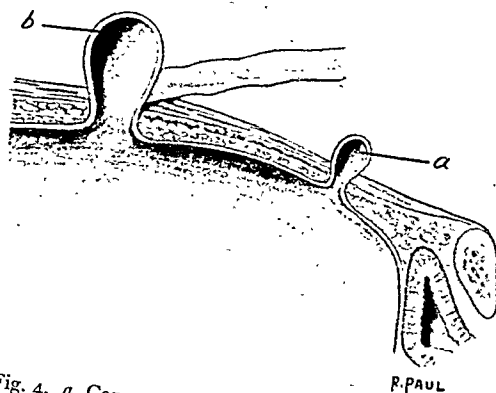


Fig. 4. *a*, Communicating diverticular locule arising independently of the indirect sac. *b*, Indirect sac.

adjacent tissues and occasionally from the bladder wall. This is a concrete illustration of the value of careful digital exploration of the entire sac and undersurface of the floor of the canal to prevent overlooking any variant of the sac or adjacent peritoneum. The locules may contain a wad of omentum which in a few instances has become incarcerated, but no bowel has yet been found within the diverticulum. Owing to the narrowness of the communicating channel, the chances of gravitation of a knuckle of bowel through this opening seems very unlikely.

The noncommunicating and communicating diverticula are structurally identical with one exception. In the former the orifice of the diverticulum has become obliterated, leaving a closed, empty, oval locule. This type of diverticulum could be very easily overlooked during the dissection of the sac. It is usually asymptomatic, and on careful examination of the canal one might elicit a small, irreducible lump; this provides for a clinical setting leading to a diagnosis of hernia, with grounds for nonacceptance industrially. Or, in the event of previous repair, these findings might be interpreted as a recurrence, when in reality, the diverticulum had been overlooked at the time of the original hernioplasty. This has occurred in 26 instances in our series.

Prior to the time we began saving and studying some of the excised diverticula in collaboration with the pathologist, we considered

them all unilocular. However, on section of some of the specimens after they had been fixed, we found one which was bilocular, the proximal locule communicating with the peritoneal cavity and the distal locule completely closed, but superimposed on the former. The combined protrusion produced a coexisting, communicating and noncommunicating diverticulum, (Fig. 1, 2).

A fatty diverticulum is a spherical, smooth, encapsulated, solitary, nonreducible mass of firm, rubbery consistency, containing packed miliary lobules of fat and making its exit through a slit in the fascia transversalis in the inguinal triangle. It is unrelated to the sac or times, the incidence being 4.8 per cent. This type of diverticulum is more prone to develop if there is considerable fatty degeneration and friable, predisposing to a tear when subjected to stress. It is a rare collateral finding in the inguinal area which, when found, should be excised with closure of the rent for the sake of completeness of the repair. Furthermore, this removal forestalls the chance of erroneous interpretation as a recurrence on later examination. An adipose diverticulum should not be confused with lipomas of the cord, which bear no immediate relation to the sac.

## DIAGNOSIS

An accurate preoperative diagnosis of diverticular hernia cannot be made. In this respect it is similar to sliding hernia, which

TABLE I.—TYPES OF COEXISTING SACS

Type	Communicating	Noncommunicating	Fatty
Direct	36	18	3
Indirect	2	3	0
Associated with recurrent direct sacs	14	20	2
Side of occurrence—			
Bilateral	2	3	0
Right side	27	11	2
Left side	11	10	1

cannot be identified as such until exposed at operation. In fact, we question the accuracy of the preoperative differentiation of indirect and direct hernias. Andrews and Bissell described and illustrated methods for their differential diagnosis, and Harris and White stressed the importance of the length of the inguinal ligament in the differentiation between direct and indirect hernias. In our experience these diagnostic maneuvers have not been successful, perhaps because of the high incidence of combined indirect-direct hernias in the age group with which we are dealing.

However, there are clinical settings which are very suggestive of diverticular hernia. The presence of a small, rather firm, irreducible bulging, about 2.5 centimeters in diameter, which transmits no impulse or a faint impulse, and, with no palpable or a dwarfed defect in the posterior wall of the inguinal triangle, is strongly suspicious of a diverticular hernia. Since a diverticular hernia rarely exists alone, the chances of a reasonably accurate preoperative diagnosis are rather remote. On the other hand, the diagnosis of such a hernia at operation is again, like sliding hernia, quite simple, as has been pointed out heretofore.

The differentiation of the diverticulum from the major sac in the communicating type is made by its size, location, and small hiatus.

TABLE II.—OPERATIVE PROCEDURES IN DIVERTICULAR HERNIAS

	Primary	Recurrent diverticula*
Routine repair	53	19
Fascial suture	2	13
Gallie or McArthur	2	0
Cooper's ligament, Dickson	0	1
Pelvic graft, modified Waujensteen	—	—
Total	62	33

\*Only recurrent hernias with associated diverticular locules included.

TABLE III.—FOLLOW-UP STUDIES

Time in mos.	Communicating	Recurrent	Noncommunicating	Recurrent	Fatty	Recurrent
3 to 12	11	3	7	0	1	0
13 to 24	18	3	6	1	0	0
25 to 36	4	0	2	0	0	0
37 to 48	2	0	4	0	0	0
49 to 60	3	0	3	0	0	0
Total	38	4	22	1	1	0
Examined by physician	28	3	11	1	1	0
Letter contact	9	1	6	0	0	0

The narrow, constricted neck never spreads or becomes dome-like, but maintains its original form after complete dissection of the sac. In fact, it is as clearcut an entity and is as easily distinguishable as a diverticulum of the bladder, with which it shares many identical characteristics. We have yet to find a diverticulum of an indirect sac, but the two may coexist (Fig. 4), the former remaining entirely unrelated to the sac. Of these there were 5 instances, or 8 per cent in this series. We have had 1 case (Fig. 2) in which the hernia was diagnosed as femoral. However, at operation this was found to be a diverticulum which had insinuated itself under the inguinal ligament between the femoral ring and Gimbernat's ligament, thereby remaining deep to the fascia transversalis and thus producing a variant in which the diverticulum did not pass through a slit in the fascia transversalis.

#### TREATMENT

In the event the diverticulum constitutes the only departure from normal, it should be excised, the stump ligated, and the tear in the fascia transversalis sutured. However, since

TABLE IV.—FURTHER FOLLOW-UP STUDIES

	No.	Per cent
Diverticular hernias in 2,302 primary hernias	62	2.6
Recurrences in 62 primary diverticular hernias	4	6.4
Recurrences in 33 recurrent hernias associated with diverticular locules	4	12.0
Diverticular locules in 130 recurrent hernias	15	13.3*

The strikingly higher incidence of diverticular locules in recurrent hernias as compared with primary hernias would indicate that the locules are being overlooked in the original repair.

\*Surg. Gynec. & Obst., 1940, 70: 969-975

the diverticulum is almost invariably concomitant with saccular and mural abnormalities, its treatment is that of the basic major weaknesses. The suitable operative procedure, therefore, may vary from the simple routine repair to the most radical hernioplasty. A summary of operative procedures used in 62 primary and 33 recurrent diverticular hernias is given in Table II. In the former, routine repair, which includes excision of the sac and diverticulum, with transposition of the cord, was done in 58 cases, or 94 per cent. In 2 instances, fascial sutures were employed, and in 2 the fascia transversalis was sutured to Cooper's ligament. In the recurrent diverticular hernias, as one would expect, the diverticula are more difficult to expose and require more formidable procedures. Routine repairs were performed in 18 cases, or 56 per cent, fascial sutures in 13 cases, or 40 per cent, and pedicle graft in 1 case, or 3 per cent. The incidence of recurrence in 62 primary diverticular hernias followed from 3 months to 5 years has been found to be 6.4 per cent (Table III). Most of these repairs were of 2 years' duration. In the diverticular recurrent hernias, the incidence was 12 per cent.

#### CONCLUSIONS

1. Data are presented showing the incidence of diverticula in 2,302 primary hernias.
2. The presumptive clinical manifestations for making preoperative diagnosis and the characteristic findings at operation are discussed.
3. The relation of the diverticulum to the coexisting sac in 62 primary and 33 recurrent hernias with diverticula is summarized.
4. Comparison of incidence of diverticula in primary and recurrent hernias is 2.6 per cent and 13.8 per cent, respectively, warranting the assumption that diverticula are overlooked at the time of the initial repair.
5. A classification of inguinal hernias on the basis of the locule and of diverticular locules is proposed.

6. The operative technique used in the primary diverticular hernias and in the recurrent hernias with diverticula in this series is detailed with follow-up studies, showing a recurrence of 6.4 per cent in the former and of 12 per cent in the latter.

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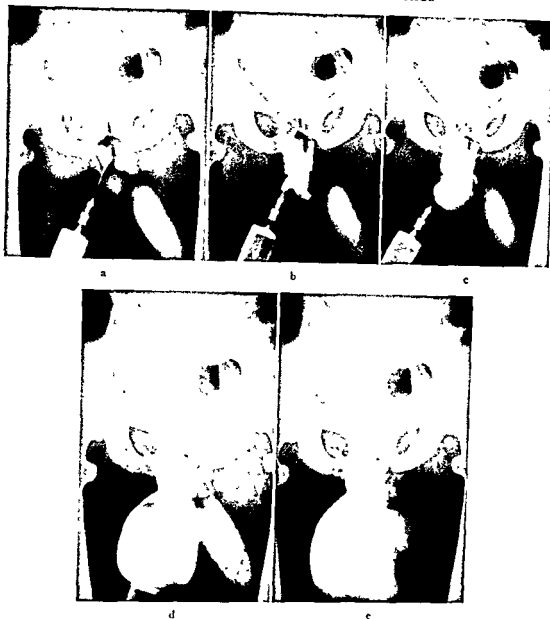


Fig 3 a, Note calcified iliac and femoral vessels. catheter in urethra, needle in perineum, where 3 cubic centimeters of iodide have been injected. b, After injection of 50 cubic centimeters the perineum is filled and there is beginning extension over the postero-inferior aspect of the scrotum. c, After injection of 150 cubic centimeters perineum completely filled, scrotum symmetrically distended mildly.

Two inguinal projections represent infiltrations along spermatic funiculi. d, After injection of 250 cubic centimeters the perineum remains the same, but there is progressive distention of the scrotum. e, After injection of 350 cubic centimeters perineum still the same, and greater distention of scrotum. No penile or abdominal involvement is seen in any of the films of this series.

asation, the rationale was to prevent more urine from being squeezed out into the tissues. On the basis of this reasoning many surgeons have failed

to divert the urinary stream when stricture or retention was absent. In fact, many prominent urologists (14, 15, 16) do not mention this pro-

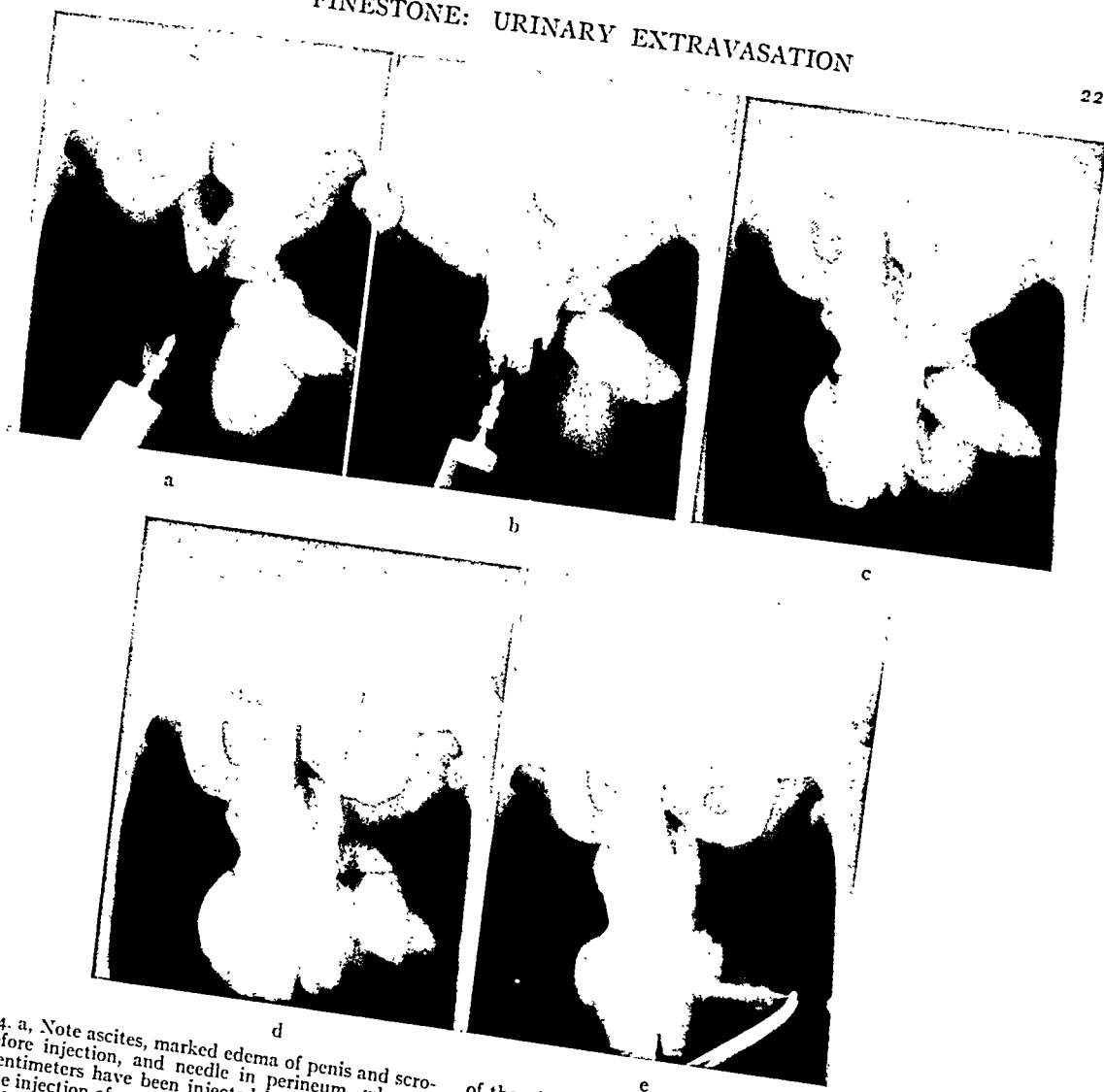


Fig. 4. a, Note ascites, marked edema of penis and scrotum before injection, and needle in perineum, where 3 cubic centimeters have been injected below the bulb. b, After the injection of 50 cubic centimeters the perineum is filled and the fluid surrounds the root of the penis and starts down the scrotum. c, After injection of 150 cubic centimeters the perineum is filled to the same extent, but only half

of the edematous scrotum is infiltrated. d, After injection of 250 cubic centimeters the perineum still remains the same, the scrotum is two-thirds infiltrated and the groins are slightly involved. e, After injection of 350 cubic centimeters the scrotum is almost filled, the groins are more involved and a few ounces of iodide in the bladder show its position. No penile or abdominal involvement is seen.

cedure. The omission of urinary diversion has led to an unwarranted and high mortality. Even those who practiced diversion could not reasonably explain this procedure in patients who were obviously voiding well and presented no stricture.

#### INJECTION EXPERIMENTS

Fresh male cadavers in which the pelvis, perineum, and genitalia were undamaged were se-

lected for the following experiments: A preliminary x-ray film was made demonstrating the scrotum and penis prior to injection. The urethra was outlined by a silk woven catheter. A No. 20 needle penetrated the right side of the perineal triangle (Fig. 2) and was advanced for a distance of about  $1\frac{1}{2}$  inches. An attempt was made to retain the needle in the same position throughout the injection. A few cubic centimeters of the

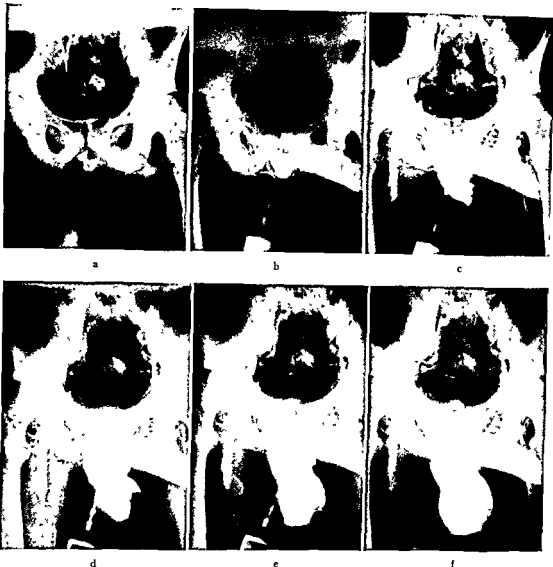


Fig. 5 a, Note inadvertent entry of bulb and initial injection of 3 cubic centimeters b, After injection of 150 cubic centimeters bulb well outlined, but no perineal infiltration, because fluid permeates vessels of perineum, penis and pelvis c, Needle slightly withdrawn, 200 cubic centimeters injected Perineum now filled Fluid starts down the scrotum Cavernous bodies and penile vessels so thoroughly

filled that the penis is one dense mass d, After injection of 300 cubic centimeters there is progressive scrotal distention e, After injection of 400 cubic centimeters there is further scrotal distention f, After injection of 500 cubic centimeters scrotum completely filled, but not as greatly distended as in series 1 and 2, because most of fluid escaped into the vascular tree

radio-opaque solution (10 per cent sodium iodide) were then injected and another x-ray film taken to demonstrate the position of the end of the needle and the site of the initial infiltration. Thereafter, injections were made of 50, 150, 250, 350 and 450 cubic centimeters, and at each incre-

ment the physical condition was noted and another x-ray film exposed

By means of a manometer the pressure reached during the injection period was measured and it was maintained at between 60 and 80 millimeters of mercury.



Fig. 6. a, Initial injection of 3 cubic centimeters into perineum with involvement of bulb. b, After injection of 100 cubic centimeters, bulb and perineum outlined. Permeation of corpus spongiosum to glans penis. Perineal and pelvic vessels filled. c, Needle slightly withdrawn; 200 cubic centimeters injected. Perineum filled. Beginning extension to scrotum. Corpus spongiosum more densely out-

lined. d, After injection of 300 cubic centimeters there is progressive scrotal infiltration. e, After injection of 400 cubic centimeters there is further scrotal distention. f, After injection of 500 cubic centimeters the scrotum is filled. Concave indentations represent the sites at which the scrotum rested upon thighs, and do not picture the testes.

Nine cadavers were injected by this method. The first case is typical of extravasation beginning in the superficial perineal pouch, derived from rupture of the bulbomembranous urethra. The first roentgenogram (Fig. 3a) demonstrates the calcified iliac and femoral vessels, a silk woven catheter in the urethra as far as the prostate, the needle in place just below and behind the urethral

bulb, and 3 cubic centimeters of sodium iodide injected. Fifty cubic centimeters of iodide were then easily injected under a pressure of 60 to 80 millimeters. The perineum now showed slight bulging, but the scrotum appeared to be the same size and preserved the rugosity of its skin. An x-ray film (Fig. 3b) at this stage revealed almost the entire perineum with exception of the root of



Fig. 7 Note marked resemblance between this clinical case of urinary extravasation and the result obtained in Figure 3 by injection. Both present symmetrical involvement of the perineum, scrotum, and groins without involvement of the penis.

the penis to be filled with the radio opaque solution which was beginning to extend forward over the posterior and inferior aspect of the scrotum. After the injection of 150 cubic centimeters typical swelling of the perineum was noted with some distention of the posterior and inferior aspect of the scrotum which began to lose its rugosity. An x-ray film (Fig. 3c) at this stage showed complete filling of the perineum and slight, symmetrical, and complete filling of the scrotum. Two horns were now evident as projections on each side toward the inguinal regions, the right one being longer and more tapering. These projections represented infiltration along the spermatic funiculi. After injection of 250 and 350 cubic centimeters,

the perineum remained swollen to the same extent as after 150 cubic centimeters, but the scrotal sac appeared progressively enlarged, more tense, and glossy with a loss of its rugosity. However, on physical appearance there was still no swelling of the penis or abdominal wall. X-ray films (Figs. 3d and 3e) made at these two stages revealed the persistently uniform distention of the perineum with the progressive enlargement of the scrotum and the two projections toward the groins.

None of the x-ray films in this series (Fig. 3) showed any involvement of the penis or the lower abdomen with the exception of the groins. Similarly, none of the films of this series showed any involvement of the vascular tree, which was a frequent and inadvertent accident in 4 of the 9 cases injected.

On dissection of the first case the blue fluid was easily traced from the confines of the superficial perineal pouch forward over the scrotal sac where it was found in the loose areolar tissue beneath the dartos. No blue was found in the deeper tissues of the scrotum nor in the tunica vaginalis testis. No blue was found in any of the layers of fascia of the penis, nor was there any blue within the corpus cavernosum or spongiosum. Blue was found extending around the loose areolar tissue surrounding both spermatic funiculi as high as the external inguinal rings, but no blue was found on the anterior abdominal wall, nor in any of the other fascial spaces in or about the bladder.

A glance at Figure 7 will show the marked resemblance between this clinical case of urinary extravasation and the result obtained in Figure 3 by injection. Both present symmetrical involvement of the perineum, scrotum, and groins without involvement of the penis. However, because the penis and lower abdominal wall are so frequently involved clinically, further attempts were made by the same technique. In the second case (Fig. 4), although the tissues were extensively infiltrated (patient had died with anasarca and marked scrotal edema), the injection fluid pursued the same course as in the first case, and none of it entered the penis or lower abdomen as demonstrated by inspection, dissection, and x-ray examination.

Of the 9 cases injected, the needle inadvertently entered the vascular tree in 4 cases. This modification of the results obtained is illustrated in the third (Fig. 5) and fourth (Fig. 6) cases. In these 2 cases x-ray films were made after injection of 3 cubic centimeters, and then after increments of 100 cubic centimeters. There was very little swelling of the perineum even after injection

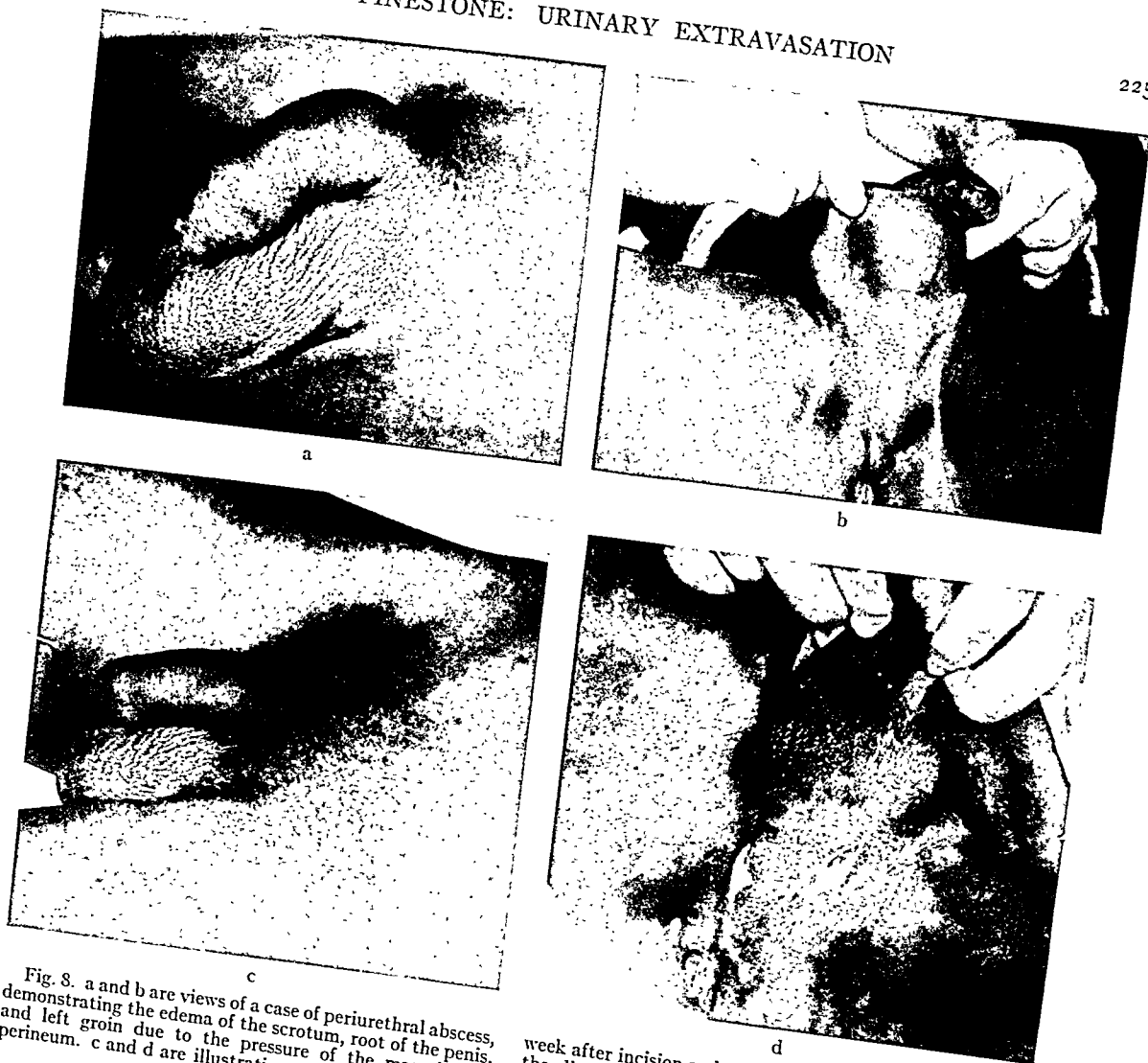


Fig. 8. a and b are views of a case of periurethral abscess, demonstrating the edema of the scrotum, root of the penis, and left groin due to the pressure of the mass in the perineum. c and d are illustrations of the same patient 1

week after incision and drainage were carried out revealing the disappearance of the edema when the pressure was released. (This is not the usual mechanism in urinary extravasation.)

enlarged nor distended, since the tissues themselves were not infiltrated.

#### EVALUATION

Cystometrically, the normal expulsive pressure on voiding has been found to be between 60 and 80 millimeters of mercury. With irritative lesions a hypertonic bladder is characteristic and the pressure on voiding still higher. The pressure required in most of the injection experiments was also between 60 and 80 millimeters, so that the hydrostatic theory for infiltration of superficial perineal pouch and scrotum seems confirmed.

of about 250 cubic centimeters and practically none in the scrotum until after about 350 cubic centimeters, because from the very beginning the iodide had entered the vascular tree, outlining the iliac vessels and all their tributaries. The perineum and scrotum were distended later, because the needle was withdrawn slightly after several hundred cubic centimeters had been injected. This demonstrates the ease with which the vascular system may be entered, although the fluid was always injected under light pressure. Even though the vessels and cavernous bodies of the penis were densely injected, this organ was not

It is interesting to note that in none of the cadavers injected was any swelling of the penis or lower abdomen demonstrated by inspection, palpation, roentgenogram, or dissection. Even when the vascular tree had been entered, the fluid was confined to the vessels and cavernous bodies. This discrepancy between the clinical appearance in some cases of extravasation and that obtained experimentally by primarily infiltrating Colles' pouch is important.

The ease with which the vessels were entered suggests several factors which are operative in the live subject: Another glance at Figures 1 and 2 reveals that all periurethral inflammations or lesions must first penetrate the very vascular bulb or part of the spongiosum to reach the superficial perineal pouch. In this passage from urethra to fascial space they invariably involve the vascular tree, thereby easily setting up a vascular thrombosis or thrombophlebitis. Anterograde or retrograde extension of this process is favored by the contractions of the bulbocavernosus and external sphincter muscles, which are brought into play with each act of voiding. This explains the paradox in which the condition of extravasation is aggravated in those patients who continue to void. Moreover, this concept of the pathogenesis explains the development of extravasation without stricture or obstruction, and also the urgent necessity for diversion of the urinary stream, irrespective of whether the patient is voiding well or not. These muscles must be put at absolute rest to prevent them from squeezing the thrombosed bulb, and thereby extending the process into the scrotal and penile vessels.

This latter process accounts for the high incidence of toxicity and jaundice, the rapid appearance of the swelling of the penis and scrotum, and the ultimate gangrene. Once extravasated urine, blood, or an abscess occupy the superficial perineal pouch, it is easy to see how the pressure of the mass in the confined space would produce vascular obstruction of the scrotal vessels without actual thrombosis. This mechanism is seen in many periurethral abscesses. When the abscess is incised, the edema disappears, because of the release of pressure (Fig. 8).

Since the subcutaneous tissues of the penis and abdomen are not involved in the cadaver (where purely a hydrostatic process is operative), it must be assumed that the difference in the living subject is due to the presence of an active circulation or of other factors. It is probable that the loss of tonicity of the scrotum allows of greater distention in the cadaver without allowing the fluid to infiltrate the penis or lower abdomen.

Lastly, but invariably, the invasion of the loose areolar tissues by organisms of variable virulence accounts for the clinical picture.

Therefore, seven factors play parts in determining the characteristics of extravasation: (1) anatomical distribution of fascial planes; (2) nature and location of urethral lesion; (3) hydrostatic pressure of extravasated fluid, (4) vascular obstruction induced by pressure of perineal abscess or extravasated fluid, (5) occurrence of vascular thrombosis or thrombophlebitis, (6) elasticity, tonicity, and contractility of the tissues and muscles, (7) nature of the invading organism.

#### SUMMARY

In summarizing the facts gleaned from our experimental, bacteriological, and clinical knowledge, the two opposing theories for the pathogenesis of extravasation may be now balanced and perhaps correlated. In this connection, I believe that the condition known as "idiopathic scrotal gangrene" is only another form of urinary extravasation or periurethral phlegmon. All the reports (5, 8, 19, 22) on this mysterious condition use only one criterion in differentiating it from periurethral phlegmon, namely, the absence of stricture or obvious urethral lesion. In the light of the present study, idiopathic scrotal gangrene is easily explained without stricture or obvious urethral lesion.

#### FACTORS FAVORING HYDROSTATIC THEORY

1. Anatomically, Colles' fascia allows a progressive infiltration of the perineum, scrotum, penis, groins, and abdominal wall.
2. Kidd found a 2 per cent urea content in the fluid obtained from infiltrated tissues at operation.
3. Injection experiments on the cadaver reveal that the clinical appearances can be simulated (with the exception of penile and abdominal involvement) by using pressures and amounts of fluid comparable to those which are expected on voiding.
4. Cystometrically, the normal expulsive pressure on voiding varies between 60 and 80 millimeters of mercury. With irritative lesions a hypertonic bladder and still higher pressures are characteristic.
5. Pressures required in injection experiments were between 60 and 80.
6. The incidence of stricture and urethral trauma as reported by most observers is high.
7. The incidence of anaerobes as reported by observers of both periurethral phlegmon and idiopathic scrotal gangrene is low.

8. The following explanation is advanced for the paradox that the worst cases encountered are in those patients who continue to void: (a) Attention is not directed to the necessity for diversion of the urinary stream because of the absence of retention. (b) If abscess, stricture, or rupture of the urethra produces complete retention, extravasation may not occur (and diversion is practiced early). (c) But when abscess, stricture, or rupture of the urethra does not completely shut off the urinary stream, extravasation may occur; and the increased hydrostatic pressure necessary to overcome the obstruction may force urine into the tissues at the site of the defect in the urethra.

9. Voiding "squeezes" more urine into the tissues.

#### FACTORS FAVORING THEORY OF BACTERIAL INVASION AND VASCULAR INVOLVEMENT

1. Wolfer has proved that the injection of sterile urine will not produce this process, so that in the final analysis all cases are due to infection.

2. Albarran and Cottet maintain that actual urinary infiltration does not exist, that periurethral phlegmon is due to bacterial invasion only, especially anaerobes, and that the fluid in the tissues resembling urine is an acute inflammatory exudate.

3. Eisendrath and Rolnick claim that "50 per cent of cases present no obstruction to passage of the sound, and no stricture is found, and apparently there is no loss in the continuity of the urethra; 25 per cent have intact urethras and 25 per cent present impermeable strictures."

4. As regards the low incidence of anaerobes, it can be pointed out that anaerobic cultures were not made routinely in any series.

5. The following explanation is offered for the paradox that the worst cases encountered are in those patients who continue to void: (a) The very vascular bulb surrounds that part of the urethra most frequently involved in stricture, abscess, or trauma. (b) All periurethral inflammations must first penetrate the bulb or corpus spongiosum to reach the superficial perineal pouch. (c) In this passage from urethra to fascial space, they almost invariably involve the vascular tree; thereby easily setting up vascular thrombosis or thrombophlebitis. (d) These latter developments account for the high incidence of toxicity and jaundice, the rapid and enormous swelling of the penis and scrotum, and the ultimate gangrene.

6. Voiding "squeezes" more toxic products into the circulation and propels the thrombotic or thrombophlebitic process along the scrotal and penile vessels.

#### CONCLUSIONS

1. A newer concept of the pathogenesis is based on vascular involvement.

2. This concept not only explains the varied clinical syndromes encountered, but also yields a basis for rational treatment.

3. Diversion of the urinary stream is essential even in the absence of urinary obstruction.

4. Injection experiments conducted by x-ray and dissection together with clinical and autopsy records (13) failed to reveal any case wherein the tunica vaginalis testis was involved. Therefore, the avoidance of the deeper structures of the scrotum and especially the tunica vaginalis testis is stressed as a prevention of unnecessary mutilation.

I wish to express my sincere appreciation for the kind co-operation extended to me by Dr. Solomon Weintraub, pathologist, and Dr. William Snow, roentgenologist, Harlem Hospital.

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# NEW FACTORS OF CLINICAL SIGNIFICANCE IN THE STUDY OF HUMAN SPERMATOZOA

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THE problem presented by a couple complaining of infertility is never adequately investigated until the husband's seminal fluid has been examined. In con-junction with efforts to relieve infertility in gynecological patients, seminal fluid specimens have been examined from the husbands of 58 infertile couples. It seems worth while to report the results of these observations and to point out certain interesting and heretofore not appreciated factors involved in studying human sperm.

It is my custom to instruct the husband in detail about the procedure to be followed in obtaining sperm. The material is collected at coitus in a fishskin condom, rubber condoms are avoided because of the well-known tendency for spermatozoa to be killed by the action of the rubber or by the powder used in preserving the condom. If sex contact has been indulged in with great frequency, several days' continence are advisable prior to obtaining a specimen. The material is kept at body temperature and is observed in the laboratory within 1 hour of ejaculation. The gross appearance of the sperm and its amount are recorded. Microscopic study of the motility at this time gives a rough estimate of the motility and the number of spermatozoa but is unsatisfactory for estimating abnormal forms unless they are present in large numbers.

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Fig. 1. Unretouched photomicrograph of a normal spermatozoon. The nuclear head is covered by, A, the acrosome and B, the postnuclear cap. The neck, C, is between the nuclear head and the midpiece or body, D. At posterior end of midpiece pore is the shrunken ring centrodome E, beyond which is the flagellum or tail, F. X700

A spermatozoal count should be computed of every sample of seminal fluid, and a morphological study should be made of at least one specimen from almost every patient. There is a common feeling that the number of spermatozoa and their morphology is of no great significance provided there are "sufficient motile spermatozoa" in the fresh drop. This attitude is unfortunate because sperm counts and spermatozoal morphology can be rechecked quantitatively with a considerable degree of accuracy and give us our best gauge for estimating improvement and for comparison with earlier studies. The count may be made by using a white blood cell pipette and the usual Neubauer hemocytometer. The specimen should stand in the laboratory for 30 minutes or longer before diluting, in order to reduce the viscosity. The material is then thoroughly mixed and a 1:20 dilution is made, as for a leucocyte count. I have used a freshly prepared 0.5 per cent azochloramide solution in water as a diluting fluid, this gives a more even suspension than sodium bicarbonate and phenol diluents. It is essential that agitation of the pipette be gentle to insure against fragmentation of the spermatozoa and continued long enough to assure an even mixture. After the diluted material is placed in the counting chamber, 5 minutes should be allotted for settling before the count is begun. The enumeration is made by ascertaining the number of spermatozoa in 80 of the smallest squares of the chamber, as for an erythrocyte count. To the total thus obtained six cyphers are added to compute number of spermatozoa in 1 cubic centimeter of seminal fluid.

When the count is completed, the remainder of the fluid in the pipette is smeared upon clean slides, as in preparation of a thin blood smear. If there has been a notable deficiency in the number of spermatozoa, a second series of smears is made with varying dilutions of sperm and diluent so that one slide may be obtained with a sufficient number of properly distributed spermatozoa for a satisfactory study. These smears are fixed and stained by one of several methods, depending on the purpose for which they are to be used.

Most of the more rapid methods of staining used for bacteria are unsatisfactory for spermatozoa. Alum hematoxylin and eosin gives excellent results for routine study and counting and is not too laborious a procedure. In order to

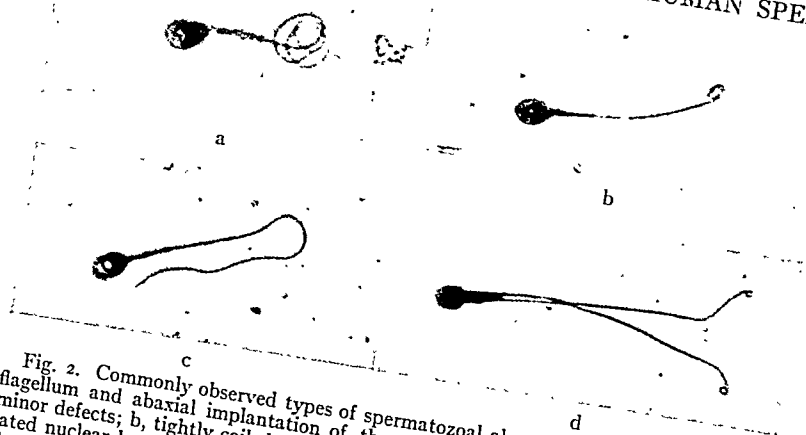


Fig. 2. Commonly observed types of spermatozoal abnormalities. a, Loosely coiled flagellum and abaxial implantation of the middle piece on the nuclear head, two minor defects; b, tightly coiled terminal flagellum, presumably an artifact; c, vacuolated nuclear head, a minor defect; d, thickened anterior centriole area and double flagellum, two major defects.  $\times 885$ .

to obtain satisfactory spermatozoal staining, it is necessary to modify the usual alum hematoxylin and eosin staining procedures for tissues as follows: (1) Dry the sperm smear in air and fix with gentle heat; (2) immerse in alum hematoxylin for 30 minutes (staining heads dark blue); (3) wash in tap water; (4) rinse in distilled water; (5) immerse in 70 per cent alcohol for 3 minutes; (6) immerse in eosin for 30 minutes (staining flagellum red); (7) rinse in 95 per cent alcohol; (8) rinse in water; (9) immerse in 95 per cent alcohol for a second time; (10) rinse in water; (11) immerse in absolute alcohol for 5 minutes; (12) clear in carboxyl xylol for 1 minute; (13) clear in xylol for 24 hours; (14) mount. When photomicrographs are to be made, this procedure is unsatisfactory, and one may resort to fixation with osmic acid and staining with Heidenhain's iron hematoxylin, using standard technique.

Two hundred or more spermatozoa in the stained preparation are examined under oil immersion and abnormalities of the nuclear head, neck, middle piece or body and flagellum are recorded. The appearance of a normal mature spermatozoon as seen microscopically is well known. It consists of a sleek, smooth, snake-like "head" to which is attached a long slender tapering tail. In stained preparations the "head" appears to consist of a large anterior and a small posterior portion, due to the presence of two thin cytoplasmic caps. The tail is divided into a thick anterior middle piece (the "body") and a thin

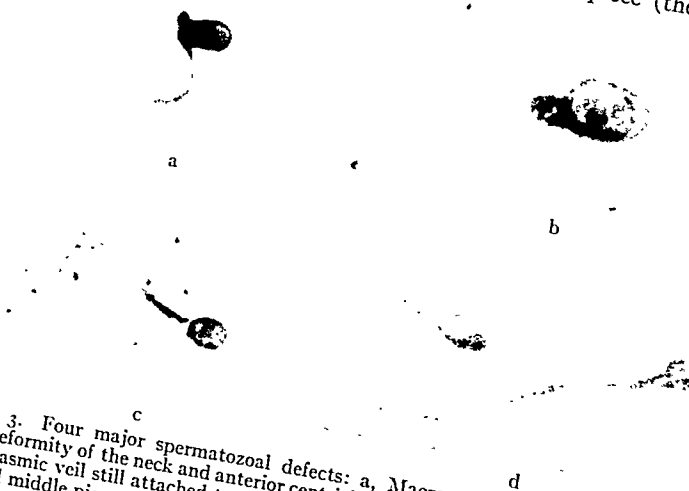


Fig. 3. Four major spermatozoal defects: a, Macrocephalic spermatozoon with gross deformity of the neck and anterior centriole area; b, tightly coiled flagellum with protoplasmic veil still attached to nuclear head; c, broken neck; d, doubled head and doubled middle piece with a single flagellum.  $\times 885$ .

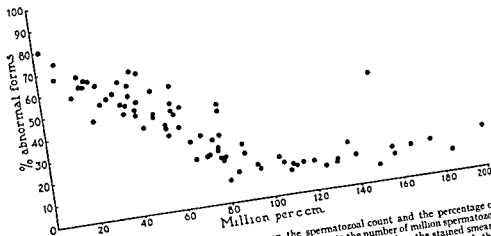


Fig 4. Graph illustrating the relationship between the spermatozoal count and the percentage of abnormal spermatozoa in the stained smear. The abscissa represents the number of million spermatozoa per cubic centimeter, the ordinate the percentage of abnormal forms observed in the stained smears. Each point on the chart co-ordinates these findings in one specimen studied. It will be noted that the percentage of abnormal spermatozoa increases as the sperm count becomes lower.

posterior flagellum, the latter making up four-fifths of this portion of the spermatozoon. A short end piece or fine filament is sometimes to be seen at the tip of the flagellum.

The intracellular structure of a spermatozoon can rarely be seen. Gatenby and Beams, in their excellently illustrated contribution have given a more comprehensive understanding of the normal morphology than was heretofore available. They state that the mature spermatozoal "head" consists of a nucleus completely covered by two caps, the acrosome in front and the postnuclear cap behind. A vacuole (Fig 2, c), the contents and function of which are unknown, is frequently observed within the nucleus. Posterior to the head is a constricted "neck." In reality this "neck" is a constricted anterior head centriole and the neck proper, which is the space between the nuclear head and the top of the middle piece. The latter, commonly called the "body" (a misnomer which should be abandoned as a structure of that name goes to make up the postnuclear cap during spermatogenesis) is, according to Gatenby and Beams, formed of a single tube upon which the mitochondria are situated. Its principal function is presumed to be concerned with propulsion of the organism. At the caudal end of the middle piece is the shrunken ring centriole, beyond which is the flagellum (or "tail").

Abnormalities in structure of human spermatozoa are of many kinds. They vary from major

#### CLASSIFICATION OF ABNORMAL SPERMATOZOA

- Abnormalities of the nuclear head
  - Microcephalic, or little head, in comparison with other organisms in the specimen being studied
  - Macrocephalic, or large head, in comparison with other organisms in the specimen being studied
  - Double head
  - Acephalic, or absence of the nuclear head
  - Irregularity of the head outline (nicks, protoplasmic excursions, etc.)
  - Rough acrosome surface (so called penetrating membrane roughness)
  - Solid staining and nonstaining heads
  - Vacuolated nucleus
  - Nuclear head still in cytoplasmic film or veil
- Abnormalities of the neck
  - Folded or acutely bent neck
  - Broken or separated neck
  - Abaxial implantation of the neck on the head
  - Swollen neck
  - Irregularity of the anterior centriole area, usually larger than normal
- Abnormalities of the middle piece
  - Broken or separated middle piece
  - Thickened middle piece
  - Irregularity of the middle piece outline
  - Folded middle piece
  - Spiral middle piece
  - Abnormalities of staining of the middle piece
- Abnormalities of the flagellum
  - Absence of the flagellum
  - Abaxial implantation of the flagellum on the middle piece
  - Double flagellum
  - Short flagellum
  - Folded or acutely bent (does not include gently curling flagellum)
  - Flagellum tightly coiled about the nuclear head

Fig. 5. Two groups of spermatozoa illustrating various types commonly seen in the stained smear. *a*, left, *A*, abaxial implantation of the middle piece on the nuclear head with enlargement of the anterior centriole area; *B*, microcephalic spermatozoon; *C*, macrocephaly; *D*, bent middle piece; *E*, enlargement of the anterior centriole area with abaxial implantation of the flagellum; *F*, swelling of the anterior

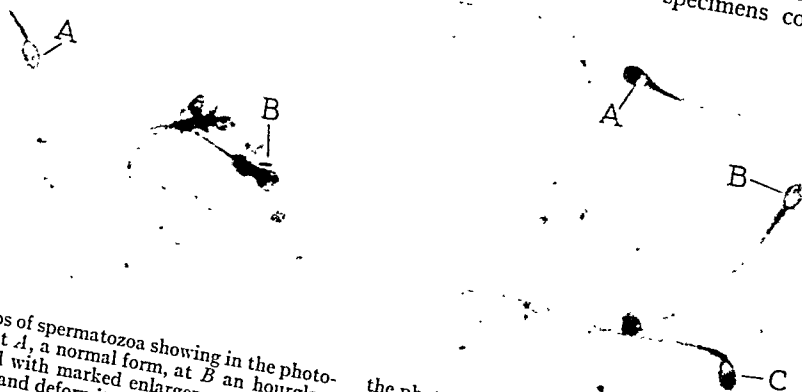
centriole area; *G*, sharply curled flagellum; *H*, marked enlargement of the anterior centriole area. *b*, right, *A*, vacuolated spermatozoon; *B*, abaxial insertion of the middle piece on the nuclear head and swelling of the middle piece; *C*, double nuclear head; *D*, thickened anterior centriole area; *E*, irregularity of the nuclear head outline; *F*, normal spermatozoon; *G*, vacuolated nucleus.  $\times 885$ .

In this study material has been examined from the husbands of 58 women who came because of their inability to achieve a pregnancy. Seventy-eight different specimens have been observed. The counts ranged from aspermia to 200,000,000 per cubic centimeter of seminal fluid and morphological abnormalities from 10 to 70 per cent in sperm containing sufficient spermatozoa to count.

A graphic record has been kept of the sperm counts and the percentage of abnormal forms in the material examined. On analysis of this graph a striking correlation between the number of spermatozoa per cubic centimeter and the percentage of abnormal forms was noted. Reference to Figure 4 will show that as the sperm count becomes lower the percentage of abnormal spermatozoa increases. In specimens containing over

self-evident deformities, such as absence of the nuclear head, to lesser defects, such as abaxial insertion of the tail into the middle piece; the latter, also lesser deviations from the normal, may or may not affect the ability of the spermatozoon to fertilize the ovum. In making these studies a modification of Moench's work has been found to be simpler and more practical.

The experience of many investigators indicates that the average number of spermatozoa per cubic centimeter of sperm is 100,000,000 and that a count of less than 60,000,000 is strongly suggestive of definite lowering of masculine fertility. It has also been a commonly accepted fact that abnormal forms should not exceed 15 or 20 per cent of the total number of spermatozoa in normal sperm.



the photomicrograph at right *A* and *B* are normal spermatozoa while *C* demonstrates the not uncommonly observed acute bending of the neck in an otherwise normal organism.  $\times 885$ .

Fig. 6. Two groups of spermatozoa showing in the photomicrograph at left at *A*, a normal form, at *B* an hourglass shaped nuclear head with marked enlargement of the anterior centriole area and deformity of the middle piece. In

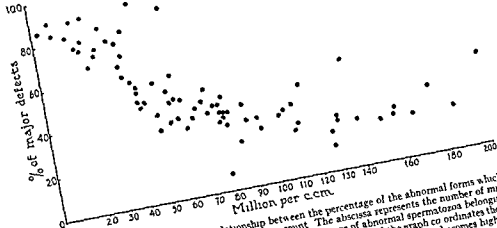


Fig. 7. Graph demonstrating the relationship between the percentage of the abnormal forms which belong to the "major defect" group and the sperm count. The abscissa represents the number of million spermatozoa per cubic centimeter, the ordinate the percentage of abnormal spermatozoa belonging to the "major defect" group observed in the stained smear. Each point of the graph co-ordinates these findings in one specimen. As count becomes lower, percentage of "major defect" forms becomes higher.

100,000,000 spermatozoa per cubic centimeter it is noted that the defective types constitute definitely less than 20 per cent of the total number of spermatozoa, in contradistinction to specimens below 100,000,000 per cubic centimeter, in which as the counts decrease the abnormal forms become more frequent. In other words, in a specimen containing 100,000,000 spermatozoa per cubic centimeter of which 15 per cent are abnormal, approximately 85,000,000 normal organisms will be available for fertilizing purposes, whereas, in a specimen containing 30,000,000 spermatozoa per cubic centimeter with 60 per cent abnormal forms only 12,000,000 morphologically normal spermatozoa per cubic centimeter can be considered functionally active. As the counts continue to decrease, there is a correspondingly greater discrepancy between apparent and real potency of the specimens.

The relative importance of various abnormalities of spermatozoal structure in decreasing human fertility remains a matter for conjecture. More than forty different abnormal forms have been described, most of which are included in the practical classification here described. Exceptions to this classification are a rarity. During the course of this investigation the types of deformities making up a preponderance of the defective spermatozoa observed in the stained smears were recorded and correlated with the sperm counts. While it is not justifiable to draw other than general conclusions from these correlations, the fact that some relation exists between the pre-

ponderant types of abnormality and the count is of great interest. It would appear logical to assume that defects of the nuclear "head" and of the neck with its anterior centriole would be more apt to interfere with proper fertilization of the ovum than would lesser peculiarities in the structure of the middle piece and the flagellum. Therefore, certain abnormalities which have been arbitrarily placed in a group in contradistinction to another group of "minor defects." In the first group have been placed those deformities which appear most likely to impair the life, the function, or the motility of the organism, among the minor defects are placed those peculiarities of structure which are questionable etiologically factors in impairing the potency of the semen, either because no reason can be given as to why they should be detrimental to the spermatozoon or because it is suspected they may be artifacts. The two groups are

## MAJOR DEFECT GROUP

- Macrocephalic abnormalities of the nuclear head
- Microcephalic abnormalities of the nuclear head
- Double nuclear head
- Absence of the nuclear head
- Broken or separated neck
- Swollen neck region
- Abnormalities of the anterior centriole area
- Broken middle piece
- Absent flagellum
- Double flagellum
- Flagellum tightly coiled about the nuclear head
- Head still in cytoplasmic veil

# MINOR DEFECT GROUP

Irregularity of nuclear head outline  
 Roughened acrosome surface  
 Abnormalities of staining  
 Vacuolated nucleus  
 Folded neck  
 Abaxial implantation of neck on head  
 Thickened middle piece  
 Irregularity of middle piece outline  
 Folded middle piece  
 Spiral middle piece  
 Abaxial implantation of flagellum on middle piece  
 Short flagellum  
 Folded flagellum

At the time the morphological studies were made the defective types observed were segregated into the two groups. The percentage of the major defect group in relation to the total number of defective spermatozoa seen on the stained slide was then determined. When this percentage was correlated with the sperm count, it was seen (Fig. 7) that as the sperm count decreases the percentage of abnormal forms belonging to the major defect group increases materially.

While it is realized that motility of the spermatozoa is of vital importance in estimating the potency of a specimen of seminal fluid, it has intentionally not been considered here. Estimation of motility constitutes a variable factor not subject to standardization. The time elapsing between ejaculation and examination, changes in temperature, and interpretation by the examiner of what spermatozoa in the fresh drop make any statement as to motility a rough approximation rather than a quantitative report. A record of the approximate percentage of motile spermatozoa per high power field in the fresh drop of the specimens reported herewith was kept, but it was felt that the addition of this factor to the present study would not enhance its accuracy and would confuse the results. It is my impression that for the most part motility will not correlate as closely with the count as the morphological variations have done. Despite this, it is imperative that a careful attempt should be made to estimate motility at the time the warm material is examined. While the movement of the spermatozoa can not be measured quantitatively, it is of utmost importance that the examiner has an impression of the approximate percentage of active spermatozoa when he places a final value on the specimen. The individual examiner will, perforce, establish his own "standard" of normality, based on experience.

## RÉSUMÉ

These observations are of interest because of the light they throw on genital function. It

would appear that when the testes excrete spermatozoa in decreased numbers, their aggregate quality becomes definitely inferior. This factor, in so far as can be discovered, has hitherto not been appreciated in evaluating seminal specimens. This would seem to be a more valid reason for careful and repeated sperm studies in clinical practice than any previously suggested. While it is no doubt true that a man of mediocre fertility, when mated with a woman of marked fecundity, may beget a child, too often there are factors in both the husband and the wife which, in combination, are sufficient to prevent gestation. It behooves us, therefore, to arrive at as exact a knowledge of both partner's procreative powers as we are able. To do this, we must do more than hazard an opinion, arrived at by cursory examination, that there are "sufficient motile spermatozoa of normal type" in a specimen brought to us for study. The knowledge that the husband has a definite decrease in his potency will, perhaps, cause treatment to be directed toward improvement in his condition. The resultant increase in his fertility may thereafter compensate for those factors affecting his wife, and pregnancy will result.

While insufficient material has been examined to warrant any definite conclusions, the abnormalities observed, when compared with the illustrations prepared by Gatenby and Beams, strongly suggest that many of these abnormal forms are in reality immature spermatozoa rather than deformities of the mature spermatozoon.

## CONCLUSIONS

As the number of spermatozoa per cubic centimeter of human seminal fluid decreases, the percentage of abnormal forms increases. Coincident with the increase in abnormal forms the types of abnormalities noted become more definitely those which would be expected to impair fertility. Semen which has a spermatozoal count definitely below normal, therefore, has a decreased potency, not only in quantity but also in quality. This observation lends added weight to the dictum that careful study of the seminal fluid is imperative in every case of human infertility. It is suggested that some of the abnormal forms of spermatozoa seen in human seminal fluid are in reality immature products of spermatogenesis.

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# RECONSTRUCTION OF THE EAR

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**R**ECONSTRUCTION of the ear has long been the *bête noire* of the plastic surgeon. This pessimism has, perhaps, been justified by the difficulty of the procedure, the length of time needed, and the high cosmetic standards required. A reconstructed ear is satisfactory only if the patient can carry out his daily routine without feeling that the fabricated organ attracts public attention.

The surgically shaped ear must be of approximately the size, shape, and angle of the normal ear. The transplantation of an amorphous blob of skin and cartilage should not satisfy the surgeon. In the past, reconstructed ears have looked

clumsy and bulky because an excessively thick tube pedicle was used for the helix. Certainly thinner tube pedicles can be made to function without loss in migration if the pedicle is delayed by undercutting and resuturing. Overzealous débridement in traumatized ears is often the prelude to an unsatisfying result. Every effort should be made to preserve the cartilage of the lacerated ear. Since in local injuries the skin will frequently retract, thus exposing the cartilage, this tissue should be thoroughly cleansed, resutured carefully, and a compressive dressing applied. Conservative treatment at this juncture saves much difficult surgery at a later date.



Fig 1a



Fig 1b



Fig 8



Fig 9



Fig 2



Fig 3



Fig 4



Fig 5



Fig 6



Fig 7

Ear reconstruction should not be attempted until the patient has attained full growth. Only at this period can proper measurements be taken from the full grown ear on the opposite side. Careful planning gives the opportunity to build an ear of about the size of its fellow.

The original flap, which goes to make up the fossa of the helix, is made in the mastoid region. This flap need not extend beyond the hairline, for if it does we are inviting the growth of hair on the ear. Nor can we evade this difficulty by the depilatory use of electrolysis or x-ray, for these procedures might jeopardize the cartilage graft.

In the 2 cases here reported, we were dealing with traumatic loss of the greater portion of the auricle following automobile accidents. Each operation was performed in 9 stages. Ether anesthesia was used during removal of the rib cartilage while local anesthesia was used during the remaining stages. In general, we followed closely the technique of George Warren Pierce. Supraclavicular skin in the form of a tube pedicle was taken for the helix. The pedicle was shifted every 3 weeks from its original site to the new fossa of the helix. A Thiersch graft from the thigh supplied skin for the back of the mastoid flap and for the skin defect in the skull. Figures 1a and 1b show the deformed ear before operation; Figures 8 and 9 indicate the operative result.

#### TECHNIQUE

*Stage 1.* The normal (left) ear was measured accurately. The new ear was outlined to scale on the right side of the patient's skull; brilliant green was used as the drawing medium. We could thus visualize the dimensions of the fossa of the helix and the height and thickness of the new helix. A piece of rib cartilage was then removed from the right costochondral junction. This cartilage was cut down to proper size and inserted in the right mastoid area directly above the external auditory meatus (Fig. 2).

*Stage 2.* A tube pedicle was made in right supraclavicular region, measuring  $\frac{1}{2}$  by 5 inches. (Fig. 2).

*Stage 3.* A curved incision was made in the right mastoid region, partly surrounding the cartilage graft. The size of this cartilage-bearing graft was only slightly larger than the fossa of the helix of the normal ear. A Thiersch graft was cut from the thigh and wrapped around a dental stent mold (Fig. 3). The dental stent was then inserted under this flap, and the flap resutured.

*Stage 4.* The medial end of the pedicle was cut and attached to the region below the lobule of ear, as indicated in Figure 4.



Fig. 10.

Fig. 11.

*Stage 5.* The cartilage-bearing flap was elevated, its lower border trimmed. The remnant of the helix on the deformed ear was cut away, but not sacrificed. The cartilage-bearing flap was then attached to the remaining concha of the deformed ear (Fig. 5). The lateral end of the tube pedicle was detached and reattached to the area directly above the tragus.

*Stage 6.* The lateral end of the tube pedicle was detached and attached to an area near the tragus. The tube pedicle now crosses the ear, as shown in Figure 6.

*Stage 7.* The pedicle was put into final position, ready to drape the new fossa of the helix (Fig. 7). Throughout all these pedicle shifts we had no difficulty with color change, edema, blebs, or other untoward complications.

*Stage 8.* At this period the tube pedicle was opened along its suture line. The cartilage-bearing flap was denuded at its borders and the helix sewed into place (Fig. 8).

*Stage 9.* As a finishing touch, the various scars were removed and the necessary modeling performed (Fig. 9).

Figures 10 and 11 show the preoperative and postoperative photographs of another ear reconstructed by the same technique. The new helix is still paler than the rest of the ear. This, in time, assumes the same coloration.

The reconstructed ear in Case 1 is somewhat closer to the side of the head than the normal ear, as indicated in Figure 9. This could have been remedied easily enough, but the patient was satisfied with the result and preferred not to have any further surgery. The operations on these patients were usually scheduled for weekends to give the patients a minimum loss of employment time. They spent an aggregate of 18 days in the hospital, each losing only 12 days from work.



# ONE STAGE OPERATION FOR CLOSURE OF LARGE DEFECTS OF LOWER LIP AND CHIN

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THE defect left after radical excision of a malignant growth of the lower lip is usually so large that transplantation of flaps either from the immediate neighborhood or from some distant parts is needed for closure. The transplantation of a flap from the upper lip into the defect of the lower lip is a simple and effective method of closing small areas (Estlander, Buck, Brown, Padgett). Larger defects require other methods, a method which is based upon the excision of two triangular pieces of cheek from the nasolabial regions (Bernard, Burow, Martin). But defects from removal of more than two thirds of the lower lip and chin cannot, as a rule, be closed satisfactorily by the latter method, particularly if the defect reaches beyond the corners of the mouth. The customary procedure to close such large defects consists of the transplantation of a flap from distant parts of the body. The lining and the lip itself are formed by skin grafting or transplanting local flaps. The disadvantages of this method are the considerable amount of time required for the procedure, the difference in skin color and texture and the loss of function. For certain defects, particularly those resulting from intensive radiation, such tube flap transplantations are the only means of closure. For primary repair, however, transplantation of local flaps can be employed with great success. The author wishes to call attention to an operation which, in his experience, is vastly superior to tube flap transplantation—an operation, as far as can be ascertained, not commonly known.

This method was originally devised by Dieffenbach, in 1834. Its principle is based upon the creation of a triangular defect which is closed by shifting two square flaps around one point of rotation from the immediate neighborhood into the defect. The two square flaps for closing the triangular defect of lip and chin in Dieffenbach's original operation reached from the corner of the mouth to the anterior border of the masseter muscles (including a small mucous membrane flap for the formation of the new lip) and from here down to the mandible. The flaps consisted of the entire thickness of the cheek. These were

shifted into the defect. The two secondary defects in front of the masseter muscles could be closed only partly and the rest was left to granulate. Remarkable as Dieffenbach's plan was, the creation of two secondary defects through the entire thickness of the cheeks, has disadvantages. It was improved by Adelmann, of Dorpat, and Szymanowski, of Kiev, in 1858. The former advised cutting broader skin flaps and in this way closing the secondary defects, at least from the outside, while the latter improved the method by leading the upper incisions not horizontally, but obliquely upward to facilitate closure of the secondary skin defects. But as far as can be ascertained no effort has been made as yet to close the muscle and mucous membrane defects in front of the masseter muscle. This triangular defect in the midst of the cheek covered only by skin is not only a source of infection but also the cause of a depression of that area. I overcame these disadvantages by transplanting a flap of the masseter muscle into the defect, as I shall describe in more detail.

## TECHNIQUE

The operation is carried out as follows:

The patient is operated upon under general anesthesia. The incisions are outlined with one of the aniline dyes. Before the anesthetic is administered I let the patient contract his masseter muscle and mark its anterior border at its upper and lower insertion with a drop of methylene blue injected percutaneously. Before operation I also mark the orifice of Stenson's duct.

*Excision of lip and chin.* The tumor, together with the soft parts of the entire chin, is excised in a heart shaped rather than a wedge shaped piece (Dieffenbach). This results later in a more normal looking profile with a dimple in the center of the chin. The patient in Figure 2d had a heart shaped excision, the patient in Figure 3a, a straight wedge shaped. If it is possible the excision should not include the entire corners of the mouth. The reconstruction of a corner of the mouth involves another problem. In those cases I leave a very small flap of the lower lip at either side of the mouth as outlined in Figure 1. The incisions on either side meet each other at a point below the

From the Lankenau Hospital, service of Dr. George P. Muller

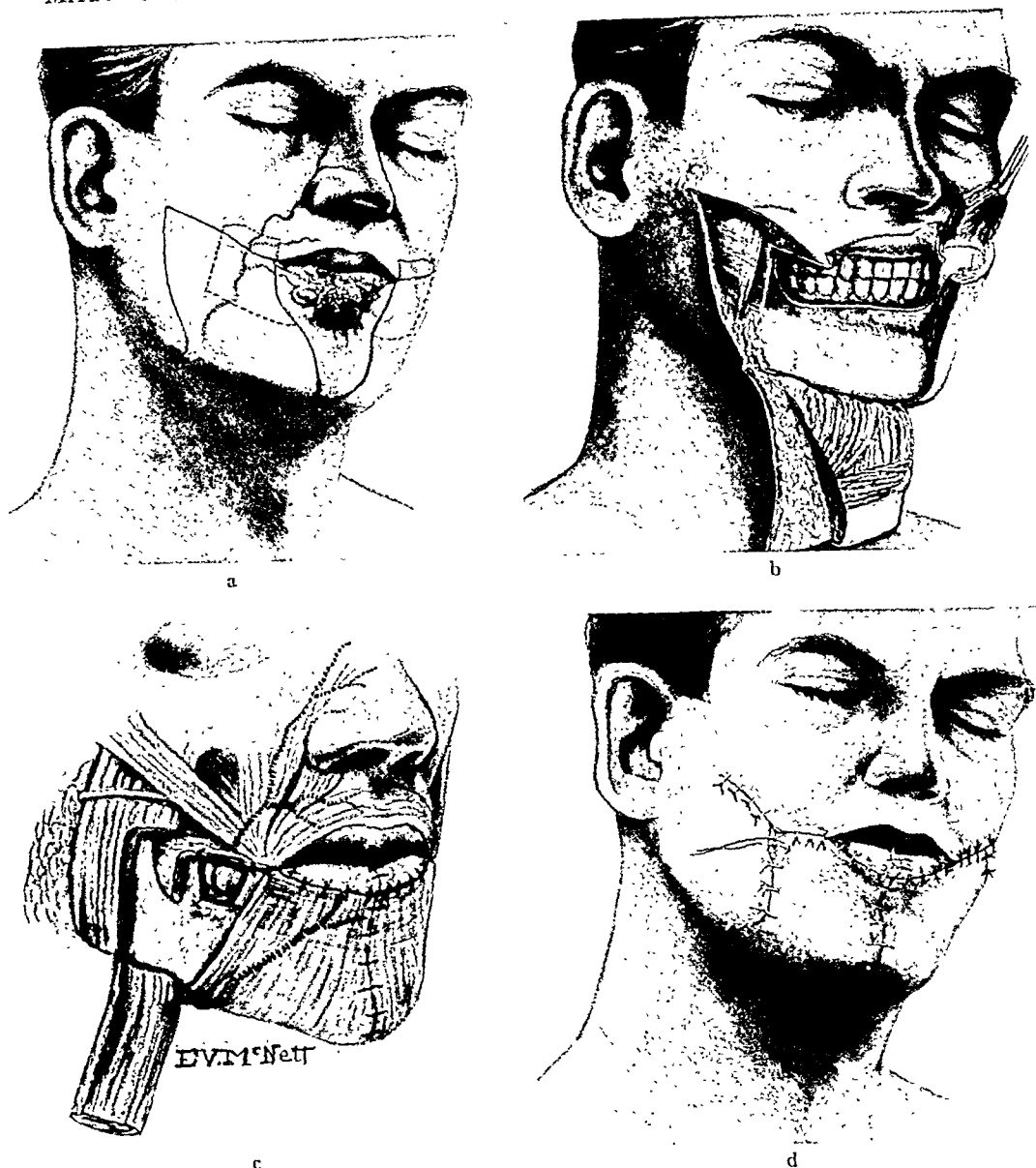


Fig. 1. a, Large cancer of lower lip; heart shaped excision of lower lip and chin is outlined, also the two square flaps which are to cover the defect; two small square flaps at corners of mouth are preserved; the inside incisions for mobilization of the flaps from the mandible and from the anterior border of the masseter muscles are outlined by dotted lines, also the small mucous membrane flaps for formation of the vermillion border. b, The right flap is mobilized; the small mucous membrane flap is sutured to

center part of the mandible. This point becomes the point of rotation around which two square

the outer edges of the main flap; the left mucous membrane flap for formation of the vermillion border is being freed. c, Closure of the triangular muscle and mucous membrane defect in front of the masseter muscle by mobilization of the mucous membrane as far as possible and transplantation of a flap consisting of the lower anterior half of the masseter muscle. The mobilization of the flap is exaggerated in this drawing for demonstration purposes. d, The original and secondary defects are closed.

flaps are turned from the immediate neighborhood (Fig. 1).



Fig. 2. a, Patient with a large squamous cell carcinoma of lower lip; no evidence of metastasis. Line of excision

outlined. b, Same patient 5 days after operation. c and d, Same patient 13 months after operation.

*Outlines of the flaps and formation of the new lip.* For the formation of the right flap—likewise the left—the following incisions are made (Fig. 1). From the right corner of the mouth an incision is carried obliquely upward to about  $1\frac{1}{2}$  inch in front of the tragus of the ear. From there the incision is carried downward at an angle less than a right angle ending below the mandible. The next step is the formation of the right half of the future lower lip. From the corner of the mouth to the anterior border of the masseter muscle the incision includes skin and muscles while the mucous membrane is dissected free from the upper wound edge for about 1 centimeter. By doing this the external maxillary artery is encountered and ligated. The facial vein is found posterior and more superficial to it

It is also ligated and separated. Still more posterior and above is Stenson's duct; care must be taken not to injure it. The mucous membrane is now separated 1 centimeter above the main flap. This tiny mucous membrane flap is now turned outward to form the right half of the future lower lip (Fig. 1b). The lateral third of this new lip, due to thickness of the subcutaneous and muscle tissue, is broader than the median parts, which results in protrusion instead of gradual disappearance of the lateral part of the vermilion border. In the first case, I had to perform a secondary corrective operation, thereafter I avoided it by excising some of the subcutaneous and muscle tissue of the lateral third of the new lip and trimming the mucous membrane accordingly. Martin also recommends this for Bernard's operation



Fig. 3a

Fig. 3b

Fig. 3. a, This patient had a squamous cell carcinoma of lower lip which was excised but recurred, radiation could not control the growth either, therefore a radical excision was performed with resection of central part of mandible, the defect was covered with a bilateral flap according to Figure 1, a to d. b, Bone transplantation was carried out subsequently. Patient 1 year after operation. c, Same patient 13 years after operation.

Fig. 4. a, Patient, aged 74 years, had a small squamous cell cancer in left half of lower lip which had been unsuccessfully treated by radiation, therefore the left half of the lower lip was excised. The defect was covered with a flap rotated from the left nasolabial region. The histological



Fig. 4a

Fig. 4b

examination, however, showed numerous cancer cells at the edges of the excised part, at least one-half inch away from the ulcer. Therefore a more radical operation had to be performed. The patient, in this figure, is shown 10 days after the first operation. The heart shaped excision is marked out, notice that one-fifth of the right lower lip was left intact, that the left side of the excision included considerable parts of the cheek, the defect was covered with a unilateral composite flap from the left side and rotation of the right cheek after triangular shaped excision of the right nasolabial region with lengthening of the lip (Burrow). b, Same patient 10 months after the operation had been carried out.

*Mobilization of the flap.* The entire flap is now mobilized (Fig. 1b). Its lateral half is mobilized by outside incisions consisting of skin only. Its median half is mobilized by inside incisions, comprising the entire thickness of the cheek. The incisions for the lateral half penetrate not deeper than to the fascia parotideo-masseterica, from which the lateral half of the flap is separated. The incisions for the median half begin with separation of the mucous membrane along its reflection at the mandible and reach from the defect to the anterior border of the masseter muscle. This incision includes the mucous membrane only. The other inside incision leading vertically upward connects this latter point with the outer edge of the newly formed lip. This incision penetrates through mucous membrane and the muscles. The entire flap is now turned downward and by blunt dissection separated from the mandible until the submandibular spaces are exposed, an important step, since the flap will not be flexible enough unless it is separated entirely from the mandible.

*Closure of defects.* Both flaps, which have surprising mobility, are shifted toward the midline into the defect. By doing this a secondary mucous membrane and muscle defect is created in front of the masseter muscle, also a secondary skin defect where the lateral half of the flap was taken. To close the muscle and mucous membrane defect I advise the following procedure: a flap of the masseter muscle consisting of its anterior lower half is separated from the underlying buccinator muscle and shifted anteriorly into the muscle defect (Fig. 1c). The closure of all defects is now carried out in the following order: connection of the lateral edge of the new lip with the corner of the mouth; connection of the mucous membrane of the flap with the gums; closure of the posterior mucous membrane defect as far as possible by mobilization of the posterior mucous membrane lip; connection of both flaps to each other in a three layer suture; connection of the masseter flap to fill the defect; connection of the lateral half of the main flap with the skin edges; closure of the secondary skin defect by starting with closure of the lateral corner. This is easily accomplished since the outer angle has been made smaller than a right angle (Szymanowski) (Fig. 1d). A drain is inserted in the lateral lower wound angle. The patient is fed through a Jutte tube.

If the tumor has involved the mandible the mandible can be resected at the same sitting after proper pre operative splinting. Dissection of glands, however, should be done in a second stage.

The same operation can be performed unilaterally for unilateral lesions; it is particularly

of value for closure of those unilateral defects whose lateral borders reach beyond the corner of the mouth (Fig. 4). If transplantation of such a unilateral flap is not enough to close the defect, it may be combined with the method of either Burow or Estlander at the other side (Fig. 4).

#### ADVANTAGES OF OPERATION

I have employed the described operation on 4 patients with extensive carcinomas of lower lip and chin. In 3 instances a bilateral flap transplantation was performed, in one instance a unilateral, combined with Burow's method at the other side. In 1 case a resection of the central part of the mandible had to be added followed by bone transplantation later. In 2 cases the regional lymph glands were subsequently dissected. The youngest patient was 34 years of age, the oldest 74. The last operation (the 74 year old patient) was performed under sodium pentothal oxygen anesthesia. The anesthesia was injected through a vein of the ankle. Thus neither the anesthetist nor the operator were in each other's way. This patient was discharged on the seventh day after operation. None of the other patients were hospitalized longer than 11 days after the operation. Primary healing resulted in all cases. In addition to the short time of hospitalization, other advantages of this operation contrasted with the tube flap transplantation are: excision of tumor and closure of defect in one sitting, replacement of lost structures by identical structures, thus restoring original function and appearance.

With this operation available there should be less tendency to carry the incision too close to the tumor when a more radical excision seems necessary to lessen any possibility of recurrences.

#### SUMMARY

A one stage operation for closure of large defects of lower lip and chin is described. The principle involved in this operation is based upon the creation of a triangular defect which is closed by shifting one or two square composite flaps from the immediate neighborhood into the defect around one point of rotation.

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# RESECTION OF DUODENUM AND HEAD OF PANCREAS FOR CARCINOMA OF THE AMPULLA

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**I**N 1935 Whipple, Parsons, and Mullins (14) reported successful resection of the duodenum and a portion of the pancreas for carcinoma involving the ampulla of Vater and head of the pancreas. Since that date 14 cases have been mentioned in the literature which have been treated by the technique described by these authors with only slight modifications. The following case is recorded as an additional example of this method of treatment:

C. C. T., Hospital No. 86,563, male, aged 47 years, was admitted to the University of Kansas Hospitals, April 24, 1940. The gall bladder and appendix were removed in 1934 followed by disruption of the abdominal wound which required 42 days to heal. Since then he has had what he calls attacks with his stomach with some epigastric distress and discomfort in the region of the right scapula. On December 26, 1939, his stomach trouble increased and he had some vomiting, his skin became yellow, and the stools were light in color. He lost 30 pounds in weight in 4 months and now weighs 128 pounds.

Examination showed that he was undernourished and jaundiced. The blood pressure was 95 systolic and 65 diastolic. There was an incisional hernia in the right upper quadrant and a slightly tender liver was felt 3 centimeters below the costal margin. A mass was not felt. There was a small right inguinal hernia. Urinalysis showed a faint trace of albumin and bile. The hippuric acid liver function test was normal. The hemoglobin was 84 per cent, red blood cells 4,280,000, and white cells 8,650. The prothrombin time was 13 1/2 seconds, clotting time 7 1/2 minutes, and bleeding time, 2 minutes. The Wassermann and Kahn tests were negative. The icterus index was 25. The blood chemistry was essentially normal with the exception of a slight decrease in the total blood cholesterol and a decrease in the percentage of cholesterol esters. The kidney function test was normal. X-ray examination was negative except for moderate dilatation of the duodenum and delayed emptying in the second portion. After 6 hours there was a slight retention of barium in the stomach.

The first stage of operation was done on April 20, 1940. The biliary tract was explored through an upper right paramedian incision. Many adhesions were encountered making exposure of the common duct very difficult. The gall bladder had been removed and the common duct was dilated, measuring 1.5 centimeters in diameter. At the ampulla there was a small firm mass about 1 centimeter in diameter, the nature of which could not be determined by palpation. The duodenum was opened and a tumor was found involving the ampulla, which was considered carcinoma. The duodenum was closed and an anastomosis was made between the common duct and the antrum of the stomach by means of a transverse incision 2 centimeters long in the duct (Fig. 1). Catgut was used for the mucosal

and fine silk for the serosal sutures. A posterior gastroenterostomy was then done, and the old incisional hernia was repaired. The patient made an uncomplicated recovery from this operation.

The second stage was carried out on May 15, 1940. Through an epigastric transverse incision, the common bile duct was ligated and sectioned, and the duodenum and a wedge shaped section of the head of the pancreas were removed. The duodenum was divided at its junction with the pylorus and through its third portion. Closure of the proximal and distal ends was made with two rows of sutures. The common duct was doubly ligated and divided about 2 centimeters above the ampulla. The V shaped wound in the pancreas was closed with interrupted sutures of silk (Fig. 1). Two small Penrose drains were placed down to the duodenal bed. The wound was closed with interrupted sutures of silk.

Gross and microscopic pathology. "The duodenum measured 7 centimeters in circumference and the specimen together with the pancreas weighed 45 grams. The external surface of the duodenum was somewhat hemorrhagic and showed a number of fibrous adhesive tags together with an adherent portion of pancreas which measures 4.5 by 4 by 1.5 centimeters. The wall of the duodenum did not appear thickened. The mucosa was light gray in color and was covered by a small amount of mucoid material. The ampulla of Vater was quite prominent. There was an elevation beneath the mucous coat which measured 25 by 12 by 8 millimeters. A probe could be readily passed from the mouth of the ampulla into a portion of the common bile duct. The bile duct appeared dilated and measured 12 millimeters in greatest diameter. The tissue around the opening of the ampulla of Vater was light gray in color, firm, and rubbery in consistency and on cut section had a somewhat cellular appearance. The attached portion of pancreas was firm and rubbery in consistency and showed distinct lobulation."

Microscopic examination showed "acute and chronic catarrhal duodenitis, chronic ulcerative cholecystitis, adenocarcinoma of the ampulla of Vater, chronic pancreatitis."

Following the operation there was a profuse drainage of clear fluid from the wound which in a few days caused definite excoriation of the surrounding skin, which was quite painful. Following the operation in 3 days the icterus index rose to 50 and on the eighth postoperative day had dropped to 15. On the second day following the second stage operation the blood amylase was 203 milligrams which dropped to 108 milligrams on the third day. Drainage from the wound was strongly positive for pancreatic ferment. Five days after the second stage the blood amylase was 75 milligrams. This gradually decreased until at the end of 30 days the amylase was 31 milligrams. At that time the icterus index had dropped to 6. At the time of discharge June 15, 1940, 51 days following the second stage operation, the wound was almost healed with only slight drainage.

He returned to the Hospital on June 28, 1940, 44 days after the operation, complaining of chills, fever, nausea, and vomiting. After admission to the hospital he did not

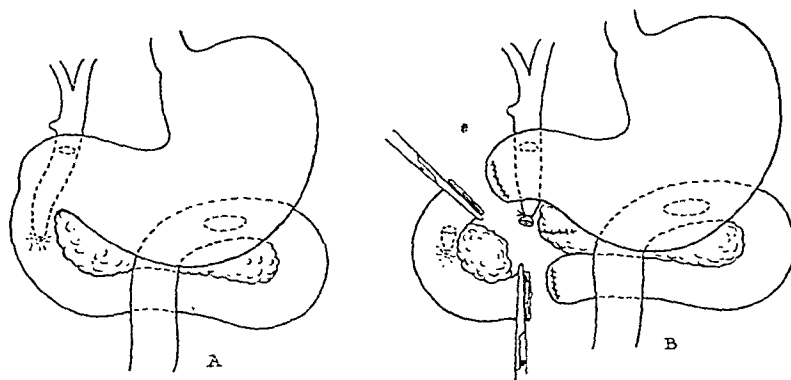


Fig. 1. a, First stage. Choledochogastrostomy and gastrojejunostomy. b, Second stage. Ligation and section of common bile duct; resection of duodenum and head of the pancreas.

have any further chills or fever and recovered from what apparently was a mild cholangitis. The icterus index was 8. In 5 days he was dismissed.

He was readmitted to the hospital a third time on August 26, 1940, complaining of pain, weakness, drainage from the wound, indigestion, and loose foul smelling stools. On July 8, 1940, he began to have colic-like pains in the epigastrium associated with clear drainage from an opening at the lower end of the scar. Drainage was profuse for several days. The opening closed spontaneously on July 14, 1940, and began draining again on July 17, 1940, and again later closed. On August 4, 1940, the fistula again opened and drained 14 days. It then closed and remained closed until after the third admission to the hospital, August 26, 1940. Two days after admission there developed a profuse flow of clear irritating fluid which was positive for amylase. There was a small mass beneath the vertical scar which was quite tender. This mass beneath the scar increased in size until it was obvious that an abscess had developed and drainage was necessary. On September 13, 1940, the abdominal wall abscess was opened and drained and the pancreatic fistula was explored. The fistulous tract led into a cavity measuring approximately 6 by 8 by 10 centimeters, extending down to the pancreas. It was completely packed with gauze and a cigarette drain was passed down beside the gauze.

When the pack was removed at the end of a week a small fistula developed from the lower ileum. Since then there has been an intermittent discharge of pancreatic juice and bowel content.

The patient lost 25 pounds following the operation which has been regained. He had occasional epigastric cramps and is very uncomfortable at times from the irritating effect of the pancreatic juice on the skin.

#### TECHNIQUE OF OPERATION

It is the general opinion at present that the operation should be done in two stages. At the first stage, as described by Whipple, Parsons, and Mullins, the gall bladder is anastomosed to the stomach, the common duct is ligated and sectioned, and a posterior gastroenterostomy is done. To minimize ascending gall duct infection Whipple (13) has more recently recommended section of the jejunum, cholecystjejunostomy, end to side

jejunojunostomy, ligation and section of the common duct, and gastroenterostomy.

At the second stage the duodenum is sectioned at or near the pylorus and through the third portion and a V-shaped resection of the head of the pancreas is done. The proximal and distal ends of the divided duodenum are closed. The duodenal bed is drained.

#### COMPLICATIONS OF THE OPERATION

Since this operation is still on trial a review of the complications encountered by various authors may be of value. The reported cases are listed in Table I.

The first case of Whipple, Parsons, and Mullins developed a duodenal obstruction at the site of a duodenoduodenostomy following resection of a portion of the duodenum with the head of the pancreas. This necessitated a third operation. A gastroenterostomy and enteroenterostomy were done. After freedom from symptoms for 7 months this patient developed abdominal pain, vomiting, chills and fever and died 8 months after operation as a result of contraction of the cholecystgastrostomy opening, liver infection, and septicemia. The second case of these authors had some discharge of pancreatic juice evident on the third postoperative day. This decreased after the eighth day, but there was still present some drainage when the patient was discharged on the eighteenth day. About 2 months after the operation sudden epigastric pain developed with vomiting, abdominal tenderness and leucocytosis. The abdomen was explored and a small pocket containing 20 to 30 cubic centimeters of yellowish fluid was found in the right upper quadrant which showed a culture of *Bacillus coli* and nonhemolytic streptococcus. The area was drained and

the patient recovered. Pancreatic juice drained from the wound for 2 weeks. This patient died 32 months after operation, with liver metastases.

Orator's patient drained pancreatic juice amounting to 300 to 500 cubic centimeters daily. On the thirteenth postoperative day nausea and vomiting developed, followed the next day by a discharge of bile from the drainage opening. On the fifteenth postoperative day the bile duct ligatures and an ascaris were found in the dressing. The ascaris was supposed to have passed through the gastroenterostomy and cholecystgastrostomy stoma into the gall bladder and bile ducts and thence through the ligatured end of the common bile duct, carrying the ligatures with it. After 4 weeks the bile flow ceased but the pancreatic flow continued. After 2 months the patient went home with a rubber tube draining pancreatic juice into a receptacle, which was emptied every few hours. Three months after the operation a jejunostomy was done and the pancreatic juice was injected into the jejunum. Later the drainage tube was connected with the jejunostomy tube, thus permitting the pancreatic juice to flow directly into the jejunum. Further progress of this patient has not been reported.

The patient operated upon by Brunschwig drained a clear serous fluid from the wound for a few days followed by a discharge of bile. The biliary drainage reached a maximum of 500 cubic centimeters daily during a period of 44 days, and then gradually diminished and became mucoid. The fluid contained food particles, indicating an intestinal fistula. Efforts to close the fistula by injection of kaolin and zinc oxide paste failed. A small fistula leading from the inverted end of the duodenal stump persisted until death. Although no metastases were found at the operation, the patient died of general carcinomatosis of the peritoneal cavity and metastases to the liver 85 days following the excision.

Trout's patient was operated upon in one stage. Death occurred in 6 to 8 hours, apparently from shock. Trout doubts the advisability of attempting the operation in one stage.

Detailed reports of the cases operated upon by Janes, Hollenberg, Schullinger, Janssen, and Whipple are not available. The results of these operations appear in Table I.

On the fourth day following the first stage of the operation Crile's patient had a hemorrhage into the intestine which was treated by several transfusions. Some fever followed which was attributed to a mild cholangitis. The cholangitis continued after the discharge of the patient at the end of 3 weeks. The night after the second opera-

TABLE I.—LIST OF REPORTED CASES OF RESECTION OF THE DUODENUM AND HEAD OF THE PANCREAS

Authors	Year Age Sex	Dura- tion of symptoms	Origin of tumor	Result
Whipple, Parsons and Mullins	1935 53 M	2 mos	Ampulla	Lived 8 mos. Died of stenosis of cholecyst gastrostomy
Whipple, Parsons and Mullins	1925 49 M	1½ mos	Ampulla	Died 33 mos. after operation with liver metastases
Orator	1936 45 F	2 mos	Papillary pancreatic carcinoma	Alive after 2 mos. No later report
Brunschwig	1937 59 M	2 mos	Ducts in pancreas	Died 85 days after operation of general carcinomatosis
Trout (Reported by Whipple)	1918 53 M	?	?	Died of shock a few hrs. after completion of operation in one stage
Janes (Reported by Whipple)	1918 ?	?	?	Died of pneumonia on fifth postoperative day
Janes (Reported by Whipple)	1918 ?	?	?	Operation successful. Late result unknown
Hollenberg (Reported by Whipple)	1918 ?	?	?	Alive after 2 mos. No later report
Schullinger (Reported by Whipple)	1918 ?	?	?	Died of pneumonia on second postoperative day
Janssen (Reported by Whipple)	1918 ?	?	Head of pancreas	Died on tenth postoperative day of septicemia and biliary fistula
Whipple	1918 ?	?	?	Died of suppurative abscess on sixteenth postoperative day
Whipple	1918 ?	?	?	Lived 8 mos. Died of liver metastases*
Crile	1915 37 M	5 mos	Bile or pancreatic ducts	Lived 6 mos. Death due to stenosis of cholecystgastrostomy stoma
Hillgorth	1910 50 M	1 mo	Probably ampulla	Died 43 days after operation with bile peritonitis
Orr	1920 47 M	3 mos	Ampulla	Alive after 6 mos. Has pancreatic and small intestine fistulae

\*Personal report by Doctor Whipple

tion the temperature rose to 100 degrees F and on the following day the patient had a chill, and the icterus index rose to 25 units. This was considered a recurrence of the cholangitis. A blood culture was positive for *Bacillus coli*. On the ninth postoperative day bile and a dye given by mouth appeared on the dressings indicating that

a gastric fistula had developed. On the eleventh postoperative day there was profuse bleeding into the fistulous tract with the formation of a large hematoma in the abdominal wall. This hematoma later became infected. The patient recovered and the fistula closed within 2 months. Death occurred after 6 months due to stenosis of the choledochogastrostomy stoma.

Illingworth's patient developed a wound infection which delayed the second stage operation. During the operation a ligature slipped off the end of the common duct which was so short that suturing was necessary. The immediate postoperative course was uneventful and the patient was out of bed in 14 days and went home in good condition. Five weeks later he developed severe abdominal pain, distention, and fluid in the abdominal cavity. Exploration was done and bile peritonitis found. Death occurred on the forty-third postoperative day as a result of bile peritonitis due to leakage from the sutured end of the common duct. The author attributes the death to a technical error in closing the severed common duct. He suggests that in the future he would implant the cut end of the common duct in the stomach.

## RESULTS

Five of the 15 patients here reviewed and reported died as a result of the operation, an immediate mortality of 33.3 per cent. Three deaths were due to metastases, 2 to stenosis of the choledochogastrostomy stoma, 1 to bile peritonitis, and 4 were alive at the time of the last report.

The effect that this operation may have upon the liver has not yet been determined. Berg and Zucker have demonstrated early degenerative changes and fatty infiltration of the liver in depancreatized dogs. They also noted extensive fatty infiltration after obstruction of the pancreatic ducts for 80 days. Dragstedt has confirmed the observation that depancreatized dogs develop fatty infiltration of the liver. These changes he has been able to prevent by administering the pancreatic hormone lipocaic. The experiments of Boyce indicate that fatty changes in the liver develop after complete or partial pancreatectomy but do not occur when the pancreas is left *in situ*. These authors suggest that in clinical cases fatty infiltration of the liver is not likely to develop when radical surgery is done for removal of the ampulla without reimplantation of the pancreatic ducts or excision of pancreatic tissue. If the head or head and body of the pancreas are excised fatty infiltration will de-

velop. Cole has called attention to fatty infiltration of the liver associated with pancreatic fibrosis. Snell and Comfort report cases of pancreatic lithiasis as a probable cause of fatty changes in the liver. With this evidence it would be logical to assume that fatty infiltration of the liver might result from resection of the head of the pancreas and obliteration of the pancreatic ducts although Whipple (14) did not find such changes at necropsy of a patient who lived 8 months after the radical removal of the duodenum and head of the pancreas.

## CONCLUSIONS

The record of patients operated upon by excision of the duodenum and head of the pancreas has been disappointing.

The plan of the operation is fundamentally sound even if the administration of lipocaic may prove to be necessary to maintain life.

A study of many more patients operated upon by this technique will be necessary before the value of the procedure can be determined.

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# THE PROBLEM OF CARCINOMA OF THE CARDIAC END OF THE STOMACH

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THE recently increasing incidence of successful resections for cancer of the esophagus has been a large factor in awakening interest in a problem in surgery which has received scant attention by the surgical profession in the past two or three decades. It is quite true that, in spite of rapid advances in the diagnostic methods of roentgenography, esophagoscopy, and gastroscopy, and improvement in surgical technique, surprisingly few attempts have been made to treat cancer of the cardiac end of the stomach by surgical means. While volumes have been written on the subject of cancer of the stomach, the scarcity of literature pertaining to neoplasms of the cardia is noteworthy. Sustained interest on the part of the medical profession in a subject such as the surgical treatment of cancer must be maintained by repeated reports of encouraging progress. At the risk of appearing repetitious, I would like to report my experience with the surgical treatment of this disease, emphasizing the fact that the diagnostic and pathological features may be quite different from those encountered in cancer of the thoracic esophagus.

From an anatomical standpoint, the cardia of the stomach may present considerable variation in size, position and shape (Fig. 1). In most individuals, the terminal one-half inch of esophagus occupies an intra-abdominal position just below the diaphragm and is known as the cardiac antrum. The mucous membrane is lined by stratified squamous epithelium. The junction of esophagus and stomach is sharply demarcated and distinct. It is indicated on the greater curvature side by an indentation called the incisura cardiaca. The musculature and mucus membrane of the stomach are thickened at the point of union with the esophagus to form a cardiac sphincter mechanism. The pars cardiaca is that part of the stomach at and just beyond the point of union with esophagus and extends over to the greater curvature side to the upper part of the fundus. The cardiac orifice of the stomach is situated at the level of the eleventh thoracic vertebra behind and the seventh left chondrosternal junction in

front. The mucous membrane of the cardia has the same columnar epithelium as the remainder of the stomach. It is important to remember that new growths in this region form adenocarcinomas in contradistinction to the squamous cell tumors arising in the esophagus.

The lymph node drainage from the cardiac end of the stomach may present considerable variation (Fig. 2). In general, the initial direction of spread is toward the nodes in the gastrohepatic omentum and also those located along the greater curvature near the incisura cardiaca. There may be further extension to the peripancreatic nodes. The latter, in my experience, is unusual. In general, it may be said that adenocarcinomas arising at the cardia spread peripherally below the diaphragm toward the gastrohepatic or gastrosplenic lymph nodes, depending upon the location of the tumor with respect to the lesser or greater curvature. However, on at least two occasions, I have seen extensive involvement of the nodes in the posterior mediastinum above the diaphragm with no enlargement of the nodes below the diaphragm. On the other hand, I have, in one case, demonstrated extensive involvement of the gastrohepatic nodes and also the liver where the primary growth was a squamous cell carcinoma located in the esophagus just above the diaphragm. I believe that experience with a great number of operative cases will demonstrate whether or not these are rare exceptions to the generally accepted interpretation of lymphatic spread from the two areas under discussion. Certain it is that early metastatic involvement of the liver is a frequent finding. It is not uncommon to discover metastatic nodules in the liver and no palpable lymph node extension. This early extension to the liver is unpredictable and is dependent upon chance invasion of the gastric veins by tumor growth and extension to the portal system.

The symptoms produced by a new growth at the cardia of the stomach will in large part depend upon the exact site of origin of the tumor and the direction of its growth. Neoplasms arising at the cardiac orifice quickly interfere with the normal act of deglutition and produce symptoms of lower substernal pain, especially on swallowing. The

growth usually extends upward to involve the lower esophagus. On the other hand, a tumor originating on the greater curvature side of the cardia near the so called silent area of the stomach may produce no symptoms whatever until it extends into the orifice itself, when difficulty in swallowing will be noted. By the time dysphagia is noted, the growth may very well have reached the inoperable stage. It is this type of case that renders the whole problem discouraging. However, it is important to stress that many of these patients may have persistent indigestion which resists ordinary medical treatment or that there may be an unexplained loss of weight. Under such circumstances, it is imperative that the physician avail himself of every diagnostic method in order to demonstrate the presence of a tumor in this region. In the main, the symptoms will depend upon the proximity of the tumor to the stream of swallowed food and the size of the growth with respect to diminution of caliber of the cardiac orifice or lower esophagus. In Case 15 in the group reported herewith, there was no difficulty in swallowing, although the tumor had grown upward to involve the lower esophagus. This was due to the fact that there was little diminution in the caliber of the cardiac orifice.

The question of loss of weight is of considerable importance to the surgeon in aiding him to estimate the probable operability of the tumor. A critical analysis of the cases reported in this paper indicates that loss of weight does not reach the extremes frequently seen in operable squamous cell cancer of the esophagus and that, when great weight loss has occurred, the tumor, in all probability, will be found to be inoperable either because of extensive node involvement or by reason of extension to the liver. Therefore, in most instances, in which a resectable growth is a probability on exploration, a preliminary jejunostomy for feeding purposes will be found unnecessary.

The symptom of persistent back pain merits some discussion. Pain in the back, of a fairly constant and dull variety and located to the left of the midline on a level with the eleventh or twelfth thoracic vertebra, is usually not an early symptom. Correlation of this symptom with the operative findings indicates its cause to be due usually to direct extension of the new-growth to the posterior parietes or to the body of the pancreas, rather than to a perigastric inflammatory reaction frequently seen with cancers in other parts of the stomach. It seems to me that this is of considerable importance in estimating operability at the time of exploration.

Possible malignant degeneration of a pre-existing benign ulcer at the cardia is of considerable interest. There were three instances in this series of a long-standing ulcer history with relief of symptoms by the usual medical therapy and in one of these the x-ray films taken 10 years previously showed clearly a small penetrating ulcer at the lesser curvature side of the cardia. In the latter case, symptoms became more persistent in the last few months and did not respond to medical therapy. While the clinical and pathological evidence of malignant degeneration of a pre-existing ulcer in these three instances is more speculative than real, the course of events in each case is certainly very suggestive.

The general examination of a patient suspected of harboring a carcinoma of the cardia rarely yields positive findings. Occasionally, one may find an enlarged lymph node in the left supraclavicular region, the so called Virchow node. Unusual hardness of this gland or fixation to surrounding tissues are indications for biopsy to demonstrate metastatic involvement. Rarely can one palpate the tumor on abdominal examination. Metastatic liver involvement may or may not be demonstrated by palpation. It is important not to omit rectal examination to exclude metastases to the rectal shelf.

It seems needless to stress that any patient presenting the symptoms enumerated should be referred to a competent radiologist for roentgenographic visualization of the esophagus and stomach. In most instances, the presence of a tumor will be clearly demonstrated by the usual methods of examination. Obstruction of the lower esophagus, irregular filling defects at the cardia, rigidity of the lesser curvature side of the cardia on fluoroscopic observation and loss of the normal mucosal pattern are among the usual roentgenographic findings. Not infrequently, it may be very difficult for the radiologist to demonstrate any abnormality. This is especially true when the tumor, usually a small one, is located on the posterior wall toward the incisura cardiaca. Persistency on the part of the examiner will, in most cases, demonstrate the growth. This will require a heavier mixture of barium and the taking of multiple films in lateral, oblique, reclining, and standing positions.

Roentgenographic examination should be followed, in every instance, by esophagoscopy. This is a most important part of the complete work-up, because the esophagoscopist is able to locate accurately the upper level of the tumor with respect to the distance from the upper incisor teeth, and thereby guide the surgeon in the choice

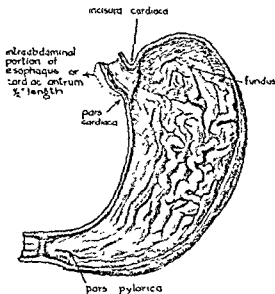


Fig. 1. Drawing of the posterior half of the stomach, anterior surface, showing the anatomical relationship of the cardiac antrum, cardia, and fundus

of his operative approach. Histological examination of the biopsy specimen which should be secured in every case will indicate the origin of the tumor from either the esophagus or the cardia.

The finding of adenocarcinoma on microscopic examination indicates origin from the cardia and will make for an altogether different plan of surgical attack than that employed when the histological picture is one of squamous cell cancer. This will be referred to later.

Up to the present time, I have preferred esophagoscopy to gastroscopy because, with the former, more accurate visualization of the tumor may be obtained and, at the same time, a biopsy specimen may be secured. In the hands of a competent operator, there is little difference in the relative risk of the two procedures.

In previous publications, I have stressed the importance of preparing these patients thoroughly for the operative ordeal. It is unnecessary at this time to elaborate on the details. Suffice it to say that this preparation should include careful attention to oral hygiene, a high caloric liquid diet containing the necessary vitamins and minerals, administration of fluids by venoclysis and a pre-operative transfusion of whole blood. In addition, as a result of our favorable experiences with the pre-operative administration of sulfanilamide in colon surgery, I have routinely administered

this drug to the patients with cancer of the cardia for 72 hours prior to operation. It is my impression that this drug is a considerable factor in minimizing infection.

The finding of adenocarcinoma in the biopsy specimen should at once indicate to the surgeon the plan of surgical attack to be adopted. I believe that there is general agreement at the present time that the operation of choice for cancer of the lower esophagus and cardiac end of the stomach with secondary esophageal extension is a left transthoracic, transdiaphragmatic resection with intrathoracic esophagogastrostomy. I believe that the combined abdominal and thoracic approach of Marwedel and the free thoracotomy technique of Ohsawa are procedures of shocking magnitude compared with the transpleural operation. Because the lymphatic spread of cancers of the cardia is in a peripheral direction below the diaphragm in most instances, it is important to determine operability without exposing the patient unnecessarily to the risks of a trans-thoracic exploration. For this reason, I recommend that exploration be carried out through a small upper left rectus incision. Palpation will quickly indicate whether the tumor is resectable. Metastases to the liver or to the pancreatic lymph nodes and fixation of the growth to neighboring vital structures are contraindications to further surgery.

If the tumor seems operable, the wound may be closed quickly with through and through steel wire sutures. The patient is now turned on his right side and, with a complete clean operative setup, the left thoracic cavity is entered through the eighth interspace. The details of the operative procedure have been described in previous publications and will, therefore, not be elaborated upon at this time. Briefly, the operation, a modification of the original Fischer and Sauerbruch procedures, includes division of the eighth, seventh, and sixth ribs close to the spine, mobilization of the distal esophagus, radial incision of the left leaf of the diaphragm, mobilization of the upper two-thirds of the stomach, resection of the tumor bearing portion, the performance of a two layer silk suture anastomosis between the end of the esophagus and the anterior wall of the stomach, and the telescoping of the esophagus into the stomach in order to minimize tension on the suture line. Under water drainage of the pleural cavity by a tube inserted through a stab wound in the subjacent intercostal space completes the operation. I believe that every patient should be transfused during the course of the operation. In every case, I have employed pos-

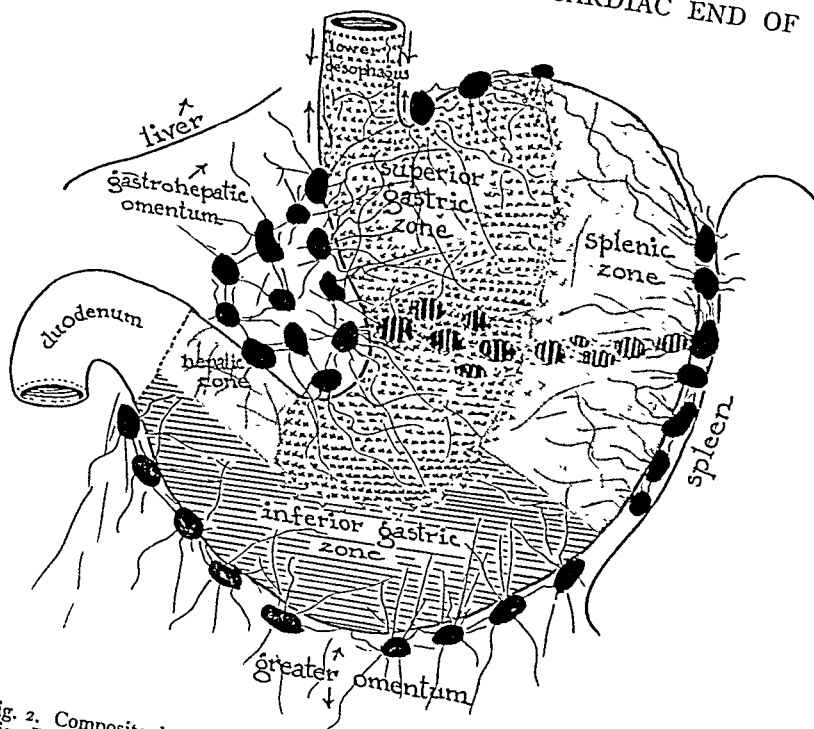


Fig. 2. Composite drawing of the lymph node drainage of the stomach taken from Poirier, Bouviere, and Cunningham, and the postmortem studies of cases of carcinoma of the cardia at Mt. Sinai Hospital.

tive pressure ethylene or cyclopropane anesthesia following a basal dose of avertin.

#### POSTOPERATIVE CARE

Before the operation is undertaken, it is important to explain to the patient that he must not swallow for a period of 4 or 5 days. The processes of repair at the suture line will be hastened by the full co-operation of the patient in this respect. Fluids are administered by a continuous intravenous drip of 5 per cent glucose in normal saline.

The character of the material draining through the intercostal tube will indicate the progress of the intrathoracic situation. During the first 48 hours, the fluid is sanguineous. After this, it gradually assumes a lighter color and decreases in amount until the seventh or eighth day when the tube may be removed.

Small sips of water may be given on the fourth or fifth day. Increasing amounts of liquid are given until the twelfth or thirteenth day when custards, gelatins, cereals, etc., are permitted. The diet is rapidly increased thereafter. Solid food should not be given until the third week.

#### RESULTS<sup>1</sup>

During the past 3 years I have operated upon 15 patients with adenocarcinoma of the cardiac end of the stomach. Five of this group were found to be operable, an operability percentage of 33.3. There was no operative mortality in the inoperable group. Five patients were subjected to the operation of resection and intrathoracic esophagostomy. Two of these succumbed: one, Case 3, of a cerebral hemorrhage on the third day and the other, Case 5, of inanition and old age debility on the fourth day. The operative mortality was 40 per cent.

The status of the 3 patients who recovered is as follows: One, Case 6, was well for 1 year when he began to develop symptoms of a local recurrence. At the present time, 16 months after operation, there is obvious metastatic liver involvement and the patient is failing rapidly. The second patient,

<sup>1</sup>Since submitting this paper for publication, I have explored 10 additional cases, making a total of 25. In the entire series, 9 were found operable, an operability rate of 36 per cent. There were 4 postoperative deaths, an operative mortality of 44.4 per cent. Of the 5 survivors, 1, Case 6 in the paper, died of retroperitoneal metastases 1½ years after the operation. The 4 remaining patients are alive and well (no evidence of recurrence) 13 months, 1 year, 3 months, and 3 months, respectively.

Case 12, is alive and well 5 months after operation. The third patient, Case 15, is alive and well 4½ months after operation.

Statistics, especially in a small series of cases, ordinarily have very little value. However, in a field of surgery such as the one under discussion, they are of considerable importance from the standpoint of indicating whether encouraging progress is being made. In addition, they indicate the risk of subjecting a patient to an extensive procedure. It is particularly important, especially in a small series, to stress that survival statistics may be materially influenced by the recovery or death of one patient.

With a disease such as cancer, there can be no half-hearted policy with respect to treatment, especially as far as our present knowledge of it is concerned. If a patient with an operable carcinoma of the cardia can be offered a 60 per cent chance of surviving an attempt at radical removal, then, I believe the risk should be undertaken. This presupposes the careful preoperative preparation and postoperative care, as already outlined. In most instances, operability must be determined by an exploration of the upper abdomen and, according to the experiences reported in this paper, the risk of this procedure is negligible.

#### CASE REPORTS

**CASE 1 C D**, male, age 56 years, was admitted to New York Hospital January 19, 1938. His past history showed that in January, 1921, he had had an operation for duodenal ulcer. This consisted of a posterior gastroenterostomy and an appendectomy. For the succeeding 8 years the patient remained in good health. He gained considerable weight during this period, finally reaching 268 pounds. He then began to experience difficulty with digestion which consisted of "our stomach" accompanied by vomiting. Occasional black stools were noted.

In May, 1931, a gastrointestinal roentgenological examination was made. The patient was told he needed another operation. He refused to have this done. Medical treatment was given at the time, with considerable relief. He had mild recurrences of epigastric distress during the intervening years.

In August, 1937, he began to experience difficulty in swallowing, and in the space of 2 weeks lost 12 pounds. This difficulty became worse until he was able to ingest fluids only. At no time had he experienced any pain.

Physical examination revealed a well-developed male. The heart and lungs were negative. There was a small upper right rectus scar. Roentgenological examination of the esophagus and stomach disclosed an irregular filling defect at the lower end of the esophagus just above the cardiac end of the stomach, with obstruction at the gastroenterostomy stoma. The barium, however, was seen to pass through the duodenum without difficulty. There was a small 24 hour residue.

On January 20, 1938, esophagoscopy disclosed marked stenosis of the esophagus due to a mass projecting into the lumen at a point 38 centimeters from the upper incisor teeth. This placed the lesion just above the cardiac end of the stomach. Microscopic examination of the biopsy

specimen taken at this time revealed papillary adenocarcinoma of the esophagus. Laboratory examinations were negative.

Operation was performed February 1, 1938—a Janeway gastrostomy. Because of the previous operation, numerous adhesions were encountered. Careful palpation of the upper end of the stomach and the upper aortic lymph nodes failed to reveal anything suggesting new growth or metastatic involvement of the nodes. Because the roentgenological examination disclosed patency of the duodenum, a gastrostomy was performed in the hope that the feedings would emerge from the stomach by the normal route.

Convalescence following this procedure was complicated by a severe lobar pneumonia involving the left lower lobe. Considerable difficulty was encountered because of reflux of gastric contents at the time of feeding. To overcome the obstruction to the flow of gastric contents through the gastroenterostomy stoma, a cystoscope was passed into the stomach through the gastrostomy opening and a small catheter was inserted through the stenotic gastroenteric stoma into the jejunum. Following this procedure the administration of feedings was greatly simplified. The patient's general condition improved and there was a considerable gain of weight.

A second operation was done on April 10, 1938. A left transpleural approach was employed. There were numerous adhesions binding the lobes of the lung to the parietal pleura and diaphragm. The mediastinum was opened and there was disclosed a neoplasm of the esophagus involving the distal 4 inches of this organ and extending through the diaphragm into the stomach. The mass was intimately adherent to the aorta and the opposite mediastinal pleura. It was considered inoperable. The chest was closed in the usual manner.

Convalescence following this procedure was uneventful. The wound healed by primary union. The patient gradually went down hill, and died of his disease at the end of May, 1938.

**CASE 2 E L S**, male, age 36 years, was admitted to Mt. Sinai Hospital, complaining of difficulty in swallowing for about 2 months. During the 6 or 7 months prior to admission, he had noted a peculiar "bursting" sensation behind the lower sternum soon after eating. This symptom had become more pronounced during the previous 2 months and was accompanied by dysphagia. During the last few weeks, he was able to swallow liquids only. Anorexia and weakness were prominent symptoms. Weight loss amounted to 12 pounds. The past history was negative.

Physical examination disclosed the following. The patient had a moderate anemia and was cachectic. There were no abdominal masses and the liver was not enlarged. There was no lymph node enlargement. Hemoglobin was 77 per cent. Red blood cells numbered 4,100,000, the white blood cells were normal. Roentgenological examination disclosed an obstructing lesion of the esophagus beginning about 1 inch above the diaphragm. Esophagoscopy (Dr. R. Kramer) showed a friable bleeding mass in the esophageal wall starting at 37 centimeters from the incisor teeth. Microscopic examination of the biopsy specimen revealed adenocarcinoma.

Operation was performed on October 14, 1938. Following a preliminary transfusion the cardia was approached through the usual left transpleural route. A very firm tumor involving the lower 2 inches of the esophagus and extending through the diaphragm into the cardiac end of the stomach was found. The tumor was solidly attached to the vertebral column and right mediastinal pleura and was therefore, considered inoperable. The thoracic wound was closed and a Witzel gastrostomy was performed.



Fig. 3. Left, Case 3. Resected cardia of stomach and lower esophagus. The lymph nodes along the lesser curvature showed metastases.

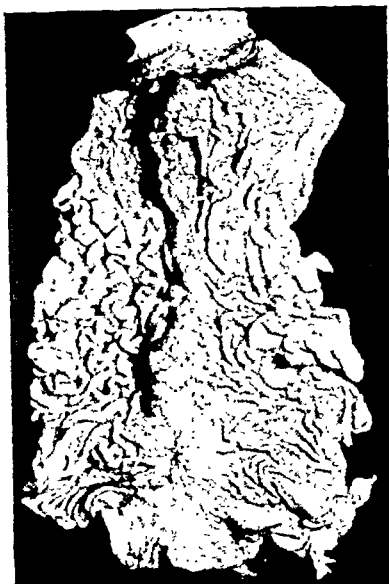


Fig. 4. Case 3. Postmortem specimen showing intact suture line.

CASE 3. J. A., male, age 49 years, was first seen January 18, 1939. He complained of upper abdominal pain of 5 years' duration. He had been under the care of numerous physicians, and many roentgenological examinations of the gastrointestinal tract had been made. He was told he had an ulcer of the stomach, and was treated medically with only transient relief. The course of events in this case suggested malignant degeneration of an old gastric ulcer, situated at the cardia. During the last 3 months, he noted persistent pain in the epigastrium radiating to the back, accompanied by marked weakness. At no time was there any dysphagia. There was a weight loss of 8 pounds. The past, personal, and family history was negative.

Physical examination revealed a rather pale, thin adult male. Heart and lungs were negative. There were no palpable masses in the abdomen and the liver was not enlarged. No enlarged lymph nodes were found. Roentgenological examination disclosed an irregular filling defect at the cardia, which extended upward and involved the lower 2 inches of the esophagus without, however, producing any obstruction. Esophagoscopy revealed a friable, ulcerating tumor beginning 37 centimeters from the incisor teeth. The biopsy specimen showed adenocarcinoma.

The patient was admitted to Mt. Sinai Hospital, January 24, 1940. Laboratory examinations showed a negative Wassermann. The urine was negative. Hemoglobin was 50 per cent; red blood cells, 3,100,000.

Operation was performed January 26, 1940. The anesthesia used was avertin-ethylene. After a preoperative transfusion of 500 cubic centimeters of blood, an incision was made in the eighth left interspace with division of the eighth, seventh, and sixth ribs close to the spine. Exposure of the lower esophagus revealed a tumor mass occupying the distal inch of the organ and extending into the cardia. The diaphragm was split radially outward from the hiatus, and exploration of the upper abdomen disclosed a normal liver and a few enlarged nodes adjacent to the cardia on the

lesser curvature side. There were no enlarged nodes in the mediastinum. Resection of the tumor was carried out after mobilization of the upper stomach and lower esophagus. The upper half of the stomach was then brought into the thoracic cavity and an end-to-side anastomosis effected between the esophagus and stomach, by means of fine silk throughout. The stomach wall was drawn over the suture



Fig. 5. Case 5. Tumor-bearing portion of cardia and lower esophagus resected at operation.



Fig 6. Case 6. Preoperative roentgenogram showing deformity at the cardia and obstruction in the lower esophagus

line and anchored to the mediastinal pleura and cut edges of the diaphragm in order to eliminate tension on the suture line. The phrenic and vagus nerves were not disturbed. The incision in the diaphragm was now repaired and the cut edges were sewn to the stomach wall. An under-water drainage tube was inserted through a stab wound in the subjacent intercostal space, and the operative wound was closed in the usual manner. The lung was now inflated. During the course of the operation, the pulse varied between 96 and 128, and the systolic blood pressure between 136 and 98. A transfusion of 500 cubic centimeters of blood was given during the operation, which took 2 hours and 20 minutes.

**Pathological examination.** The gross specimen revealed an infiltrating adenocarcinoma of the cardia with involvement of the lower esophagus. Metastatic deposits were found in the lymph nodes along the lesser curvature of the excised specimen (Fig 3).

During the first 2 postoperative days, the patient's course was most satisfactory. Pulse varied between 80 and 120, respirations, 24 to 30, temperature 100 to 102 degrees F. Fluids were administered by continuous intravenous drip. On the third postoperative day, the patient suddenly became comatose, the temperature mounted to 108 degrees F, and there were signs of a complete right hemiplegia. Notwithstanding active therapy, the patient's condition rapidly became worse, and he expired during the evening of the third day.

Autopsy examination revealed a completely expanded left lung, no evidence of infection, and an intact water tight suture line (Figs 3 and 4). Death was due to a hemorrhage at the internal capsule of the brain.

**CASE 4.** M. B., female, age 70 years, was first seen January 18, 1938. She complained of epigastric distress of 10 months' duration. The pain was experienced immediately after eating and was accompanied by hiccup. Some



Fig 7. Case 6. Photograph of operative specimen

relief had been obtained by a dietary regimen. During the last 3 or 4 months, she experienced increasing difficulty in swallowing solid food. On a few occasions, she had noted blood in the stool. She had lost 30 pounds in weight. The past and personal histories were irrelevant.

Physical examination revealed a remarkably well preserved woman. Heart and lungs were negative. Blood pressure was 160/90. No enlarged lymph nodes were present. There was resistance in the epigastrium, but a mass could not be felt. The liver was not enlarged.

She was admitted to Mt Sinai Hospital January 21, 1938. Roentgenological examination showed the presence of a mass at the cardiac end of the stomach which extended upward and involved the lower esophagus. Aside from a mild anemia, the laboratory examinations were negative.

Operation was performed January 29, 1938, under avertin ethylene anesthesia. A small upper left rectus incision was made. Abdominal exploration was undertaken first in order to determine operability. There was found a large tumor mass involving the cardia and lower esophagus. In addition, large packets of involved nodes were found overlying the aorta. The lesion was obviously inoperable. A Janeway gastrectomy was performed. The patient left the hospital and succumbed to her disease 4 months later.

**CASE 5.** L. E., female, aged 73 years, was first seen July 28, 1939. She complained of pain behind the lower sternum when eating, which had been present for over 3 months. This was frequently accompanied by hiccups. Two or one-half months ago, she noted that swallowed food seemed to stop at the point of pain. Dysphagia became increasingly more severe until she was able to swallow only liquids. The weight loss was 14 pounds. Past history was negative.

Physical examination revealed an elderly woman, in excellent general condition, heart and lungs were negative, blood pressure was 160/88, abdomen, negative, no enlarged lymph nodes. She was admitted to Mt Sinai Hospital, where a work up disclosed hemoglobin 90 per cent, red blood cells, 5,150,000. Urinalysis and Wassermann were negative. Roentgenological examination disclosed an obstructing neoplasm in the lower esophagus just above the diaphragm, with irregular filling of the cardia. Esophagoscopy (Dr R. Kramer) showed an almost completely obstructing tumor, beginning 38 centimeters from the incisor teeth. The biopsy specimen showed an adenocarcinoma.

Operation was performed August 3, 1939. Under avertin-ethylene anesthesia, a left transthoracic approach was made through the ninth interspace. There was found an

annular constricting tumor at the lower end of the esophagus and cardia of the stomach, measuring 2 inches in length. The liver was normal and no enlarged nodes were felt. The tumor bearing portion of stomach and esophagus was resected and an intrathoracic end-to-side esophagogastrostomy was carried out (Fig. 5) as described. An underwater drainage tube was inserted in the subjacent intercostal space. A transfusion of 500 cubic centimeters of blood was given during the operation. The patient stood the procedure very well. The pulse rate varied between 90 and 110. The systolic blood pressure was fairly steady at 140. Time, 2 hours and 25 minutes.

The immediate postoperative course was devoid of any untoward incident. The highest temperature, 102.6 degrees F., was noted on the third day. The pulse varied between 88 and 110, the respirations between 16 and 26. Fluids were administered intravenously. By the end of the third day, it was noted that the patient was apathetic and listless. This became more pronounced until definite coma developed on the fourth day. The patient succumbed during the evening of this day, with a terminal fever of 100 degrees F.; a pulse of 100; and respiratory rate of 16.

Postmortem examination was completely negative, except for a small localized abscess in the lower mediastinum near the suture line. The latter was quite intact. No remaining carcinoma was found.

CASE 6. W. H., male, aged 49 years, was first seen June 14, 1939. He complained of dysphagia of 6 weeks' duration and stated that swallowed food stopped at about the level of the ensiform cartilage, remained there a few moments, and then passed on into the stomach. There was no regurgitation. Fluids were swallowed with ease. The weight loss was 5 pounds.

Physical examination disclosed a well nourished individual, apparently in good health. There were no abnormal findings. Roentgenographic examination of the esophagus showed an obstructing neoplasm at its lower end, involving also the cardia (Fig. 6). He was admitted to Mt. Sinai Hospital, where esophagoscopy (Dr. R. Kramer) showed an ulcerating, obstructing tumor, beginning at 40 centimeters from the incisor teeth. The biopsy specimen showed a mucous cell carcinoma. All laboratory examinations were negative.

Operation was done June 20, 1939, under avertin-ethylene anesthesia. Left transthoracic approach was made through the eighth interspace. There was found a constricting, annular tumor involving the distal 2 inches of esophagus and extending into the cardiac end of the stomach for about 1 inch. Abdominal exploration through an incision in the diaphragm revealed a normal liver, but a number of enlarged, firm nodes in the gastrohepatic omentum and also along the greater curvature in the region of the cardia. Operation consisted of a radical resection of the lower esophagus and upper stomach with removal of as much of the gastrohepatic and gastrocolic omenta as was possible. An intrathoracic esophagogastrostomy was performed.

Pathological examination of the excised specimen showed an infiltrating mucous cell carcinoma of the cardiac end of the stomach with involvement of the lower end of the esophagus. All the excised lymph nodes showed metastatic involvement (Fig. 7).

The immediate postoperative course was uneventful. There was an initial rise of temperature to 103.4 degrees F. The patient's general condition was excellent. The swallowing of fluids was started on the sixth day. The intercostal drainage tube drained gradually diminishing quantities of serosanguineous fluid until the eighth day, when the tube was removed. The operative wound healed by primary union.



Fig. 8. Case 6. Roentgenogram of esophagus and stomach, taken 7 months after operation, showing intrathoracic position of upper stomach, (slightly retouched).

The postoperative elevation of temperature which usually persists in these cases until about the fifth day, did not subside, and remained elevated between 102 and 103 degrees F. Repeated examinations finally disclosed the presence of fluid at the right base in front and laterally. This was confirmed by roentgenological examination. Repeated aspirations were negative. There was no cough or expectoration. For a fleeting moment on the tenth day, it was thought that the breath was foul. The patient presented a peculiar dyspnea without cyanosis. The respiratory rate ranged between 26 and 40. On the twelfth day, the patient suddenly went into profound shock, with marked dyspnea, cyanosis and severe respiratory embarrassment. The physical signs were those of air and fluid in the right pleural cavity. Aspiration of the chest showed putrid air and pus to be present. An immediate wide thoracotomy was performed under local anesthesia. The patient had apparently ruptured a postanesthetic lung abscess which was peripherally located and which had not made itself manifest by the usual foul breath and sputum. The pleural effusion originally noted was of the sympathetic variety.

Convalescence following this operation was slow but progressive. The right lung expanded completely, and the wound finally healed. The patient was discharged from the hospital at the end of the sixth week.

There was a rapid gain in weight. The patient was able to swallow all types of food without difficulty until about the fourth month, when it became apparent that a stricture was forming at the site of anastomosis. Esophagoscopy showed a tight stricture at the site of the suture line. In performing a biopsy at this point, Dr. Kramer removed the



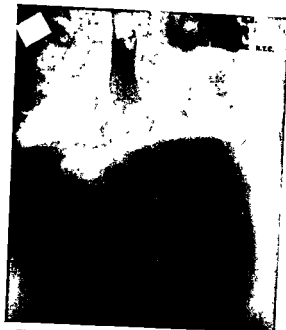


Fig 9 Case 12. Preoperative roentgenogram showing irregular, stenosing filling defect in lower esophagus and cardia.

silk thread which had been used to effect the anastomosis. Thereafter, the orifice widened rapidly and no further dilatation became necessary (Fig 8).

The patient was well until 1 year after operation. At that time, he began to experience mild substernal pain on swallowing. Esophagoscopy examination disclosed a small flat tumor on the posterior esophageal wall, about 2 centimeters above the anastomosis. A biopsy specimen showed the same histological features of carcinoma as the original growth. Dr Kramer inserted a few radium seeds in the hope of checking this lesion. However, at the present writing, 16 months after the original operation, the patient is failing slowly and losing weight. The outlook seems hopeless.

CASE 7 J B male, aged 62 years, was first seen September 27, 1939. He stated that his present illness had started 4 months before, with indigestion and belching of gas. There was no pain until the beginning of September, when he noted retrosternal distress on swallowing. He vomited occasionally, and was unable to swallow solid food. He had lost 20 pounds.

Physical examination revealed an elderly man in excellent general condition. The liver was not enlarged. There were no abdominal masses or enlarged lymph nodes. Roentgenographic examination showed a filling defect at the cardiac orifice, with marked obstruction of the lower end of the esophagus. The latter structure was markedly dilated above the obstruction.

The patient was admitted to Mt Sinai Hospital, where esophagoscopy disclosed an obstructing neoplasm, starting at 40 centimeters from the upper incisor teeth. There was a moderate anemia.

Operation was performed October 5, 1939, under avertin-ethylene anesthesia. As recommended in the body of this paper, an abdominal exploration was carried out through a

small upper left rectus incision. A tumor mass, located in the cardia and extending into the esophagus was found. It would have been considered operable were it not for the fact that metastatic nodules were found in the liver. A Janeway gastrostomy was performed. The patient left the hospital, and died 5 months later of his disease.

CASE 8 W C, male, aged 47 years, was admitted to Mt Sinai Hospital, October 20, 1939. He stated that for the past 4 years he had experienced recurrent episodes of postprandial epigastric pain, relieved usually by medication and dietary restriction. During the past 4 months he had steady, dull pain in the epigastrium with a sense of fullness and gradually increasing difficulty in swallowing solid food. He had lost 40 pounds.

Physical examination disclosed the following. The patient showed a marked recent weight loss. Heart and lungs were negative, abdomen, negative, laboratory examinations, negative. Roentgenographic examination showed a large filling defect at the cardiac orifice of the stomach, with extension to the lower esophagus. Esophagoscopy (Dr J Goldman) revealed a firm, ulcerating tumor, starting at 30 centimeters from the incisor teeth. A biopsy specimen showed adenocarcinoma.

Operation was done October 25, 1939, under avertin-cyclopropane anesthesia. Exploration of the upper abdomen was carried out through a small left rectus incision. A tumor mass was found extending from the esophageal hiatus downward along the lesser curvature for about 2½ inches. The tumor was movable and there were no enlarged nodes or palpable nodules in the liver. The tumor was considered operable. Therefore, the left thoracic cavity was opened through the eighth interspace. Exploration revealed a very extensive involvement of the esophagus with extension to the mediastinal nodes so as to form an elongated, stony hard fixed mass which was obviously inoperable. The wound was closed.

The patient's convalescence was uneventful, and he was discharged at the end of the third week. He died of his disease 3½ months later.

CASE 9 M M, male, aged 60 years, was first seen September 28, 1939, at which time he complained of difficulty in swallowing for the past 4 weeks. At the onset of his illness, dysphagia resulted from ingestion of solid



Fig 10. Case 12. Photograph of operative specimen.

food only, but it rapidly became worse until, at present, he was able to swallow only liquids. At no time had he experienced any pain. The weight loss was 10 pounds. The past, family, and personal history was negative. Examination showed an elderly man in excellent physical condition. Heart and lungs were negative; no enlarged cervical nodes. The abdomen was negative. The prostate gland was moderately enlarged. All laboratory examinations were negative.

The patient was admitted to Mt. Sinai Hospital, where the esophageal roentgenogram disclosed an obstructing neoplasm at the lower end of the esophagus, extending into the cardia of the stomach. Esophagoscopy (Dr. R. Kramer) revealed a granular, ulcerating tumor, beginning at 41 centimeters from the incisor teeth. A biopsy specimen showed adenocarcinoma.

Operation was performed October 6, 1939, under avertin-ethylene anesthesia. The left thoracic cavity was opened through the eighth interspace and the ninth and eighth ribs were divided close to the spine. There was felt a large, firm irregular tumor occupying the terminal 2 inches of the esophagus, with extension into the stomach. Throughout the mediastinum were felt large, hard metastatic lymph nodes which were fixed to the aorta and esophagus. The condition was deemed inoperable and the wound was closed. A small left rectus incision was now made, and a Witzel gastrostomy was performed. Exploration of the upper stomach showed that it was fixed by tumor tissue to the diaphragm and retroperitoneal tissues. The post-operative convalescence was uneventful, and the patient was discharged from the hospital 3 weeks later. He died of his disease soon afterward.

CASE 10. H. Z., male, aged 62 years, was first seen October 9, 1939. He complained of dysphagia of 5 months' duration. This difficulty started rather suddenly, when he noted that swallowed food seemed to stop at a point behind the ensiform cartilage. Dysphagia became progressively worse until he was able to swallow only liquids. One month after the illness began, roentgenological examination was pronounced negative. Esophagoscopy was performed by Dr. John Kernan, September 12, 1939, who found an obstructing, granular tumor, beginning about 40 centimeters from the incisor teeth. A biopsy specimen showed adenocarcinoma. The patient had lost 30 pounds in weight.

Physical examination disclosed a chronically ill man, with obvious weight loss. The left supraclavicular lymph nodes were slightly enlarged. No abdominal masses were palpable. Rectal examination was negative. On the basis of the duration of symptoms, the weight loss, and the origin of the tumor from the cardia, it was felt that the condition was probably inoperable. However, gastrostomy was certainly indicated, and exploration through the abdominal incision could be carried out at the same time.

He was admitted to Mt. Sinai Hospital, where operation was carried out under avertin-ethylene anesthesia. A large carcinoma of the cardia was found extending through the diaphragm into the lower esophagus and infiltrating the under surface of the liver. At the urgent request of the family, gastrostomy was not performed. Convalescence was uneventful, and the patient left the hospital. He died of his disease 10 weeks later.

CASE 11. C. L., male, aged 57 years, was first seen March 1, 1940. He complained of dysphagia of approximately 2 months' duration. This was accompanied by substernal distress. Difficulty in swallowing rapidly became worse until he was able to swallow only liquids. The weight loss was 15 pounds. There was considerable loss of strength but no impairment of appetite. Roentgenographic examination a week before showed an obstructing

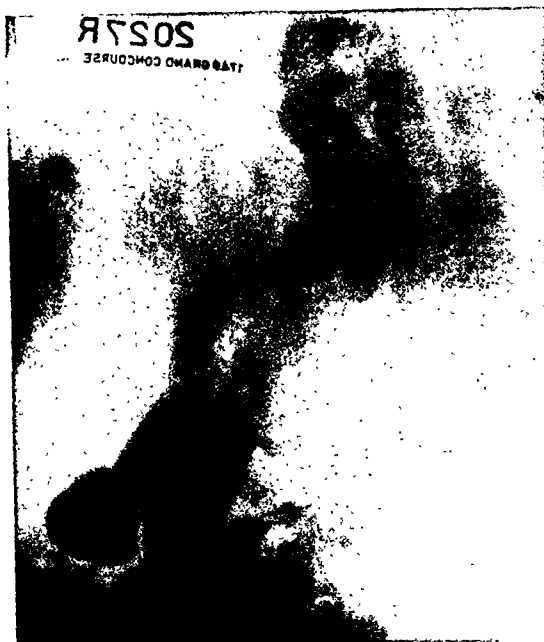


Fig. 11. Case 12. Roentgenogram of esophagus and stomach, taken 5 months after operation, showing the wide orifice at the site of anastomosis.

neoplasm in the lower esophagus and cardia, with probable extension toward the fundus of the stomach.

The past history was of considerable interest. Ten years before, he was treated for an ulcer of the lesser curvature of the stomach just below the cardia. The roentgenograms, which had been preserved, clearly indicated the lesion. Under a careful medical regimen, the symptoms abated, with a corresponding roentgenographic disappearance of the ulcer. He was symptom-free until the onset of the present illness.

Physical examination disclosed a chronically ill, moderately anemic elderly man. The cervical nodes were not enlarged. Heart and lungs were negative. No mass was palpable in the abdomen. Rectal examination was negative.

He was admitted to Mt. Sinai Hospital, where esophagoscopy (Dr. R. Kramer) disclosed an obstructing tumor of the esophagus, starting at 39 centimeters from the incisor teeth. A biopsy specimen showed adenocarcinoma. Red blood cell count was 3,300,000; hemoglobin, 70 per cent.

Operation was performed March 7, 1940, under cyclopropane anesthesia. Following a preliminary transfusion, exploration through an upper left rectus incision revealed a large neoplasm of the cardia, adherent to the under surface of the liver, to the aorta, and to the diaphragm. It was obviously inoperable. A Spivack valvular gastrostomy was performed. Convalescence was smooth, and the patient left the hospital 3 weeks later. He died of his disease after 4 months.

CASE 12. S. R., female, aged 58 years, was first seen May 11, 1940. Her main complaint was dysphagia of 6 weeks' duration. About 5 months before, she had had an attack of biliary colic which was followed by anorexia. The onset of dysphagia was not associated with pain or vomiting. Swallowed food seemed to stop at a point behind



Fig 12 Case 15. Preoperative roentgenogram showing the finger-tip deformity of the cardia and upper fundus

the ensiform cartilage. There was marked anorexia, and a weight loss of 10 pounds. The patient had suffered from diabetes mellitus for 12 years, and was taking 30 units of insulin daily.

The family history was interesting from the fact that three brothers and two sisters had died of cancer of the breast, liver, stomach, tongue, and stomach, respectively.

Physical examination disclosed an elderly woman, in good general condition. Heart and lungs were negative. Abdominal examination showed enlargement of the liver two fingerbreadths below the costal arch. The edge was sharp and the surface was smooth. No masses were palpable. Lymph nodes were not enlarged. Rectal and pelvic examinations were negative. Roentgenograms submitted by the patient's son, who is a physician, disclosed an irregular stenosing filling defect in the lower esophagus just above the diaphragm (Fig 9). Laboratory data: red blood cells numbered 5,000,000, hemoglobin, 100 per cent, blood sugar, 135 milligrams per cent, urine, negative.

She was admitted to Mt Sinai Hospital May 15, 1940. Esophagoscopy (Dr R Kramer) showed an ulcerating, stenosing neoplasm, starting at 36 centimeters from the incisor teeth. A biopsy specimen showed adenocarcinoma.

Operation was performed May 21, 1940, under avertin-ethylene anesthesia. In order to determine operability, a small left rectus incision was made. Palpation revealed a neoplasm at the cardiac end of the stomach with extension upward into the esophagus for about 1½ inches. A few enlarged lymph nodes were felt in the gastrohepatic omentum near the cardia. The liver was normal. The tumor was deemed operable and the wound was closed with through and through steel wire sutures. The patient was placed on the right side and the left thoracic cavity opened through the eighth interspace. The eighth, seventh, and sixth ribs were divided close to the spine. The lower 2 inches of esophagus were involved by the new growth. One enlarged mediastinal node just proximal to this point was



Fig 13 Case 15. Photograph of operative specimen

removed. The diaphragm was split and the stomach was mobilized by dividing the left gastric and gastroepiploic vessels. The tumor bearing portion of stomach and esophagus was removed with as much of the gastrohepatic ligament as was feasible. An intrathoracic end-to-side esophagogastrostomy was now performed, two layers of fine silk sutures were used. The stomach was telescoped over the suture line and anchored to the mediastinal pleura and diaphragm. The latter structure was closed about the transplanted stomach. A stab-wound was made in the sub-jacent intercostal space for an under water drainage tube, and the operative wound was closed.

During the course of the operation, which consumed 2 hours, a transfusion of 750 cubic centimeters of blood was given. The pulse varied between 90 and 138, and the systolic blood pressure between 148 and 98.

The resected specimen showed an infiltrating adenocarcinoma of the cardiac end of the stomach with involvement of the lower esophagus. Only one node showed metastatic carcinoma (Fig 10).

The first day after operation the temperature was 102.8 degrees F, respiration, 24, pulse, 120. Singuineous fluid discharged through tube. The second day after operation the temperature was 104 degrees F, respiration, 24 to 32, pulse, 118 to 126. The fourth day, temperature was 101 degrees F, respiration, 20, pulse, 116. One dram of water was swallowed every half hour without difficulty. Amount of fluid swallowed was rapidly increased thereafter. From the first day, a continuous intravenous drip of 5 per cent glucose in saline was maintained supported by the necessary amount of insulin. Dr S S Bernstein cared for the diabetic condition. The seventh day, temperature was

100 degrees F.; respiration, 22; pulse, 84. Little discharge came through the chest tube. The operative wounds were clean. All sutures were removed. On the ninth day after operation the chest tube was removed. Temperature was normal, and patient was taking fluids well. On twelfth day phlebitis of left leg with marked edema up to knee was noted. General condition was excellent. Blood sugar was 115 milligrams per cent.

The subsequent course in the hospital was one of continued improvement. The phlebitis subsided completely, and the urine remained sugar-free. The patient was swallowing most foods by the twenty-first day. Upon discharge, June 22, 1940, the hemoglobin was 70 per cent, and the red blood cells numbered 3,800,000.

It is now 5 months since operation. She has regained her lost weight. She swallows all types of food without difficulty and, what is most difficult to explain, she is free of all symptoms of diabetes mellitus and no longer needs insulin (Fig. 11).

CASE 13. H. S., male, aged 67 years, was first seen June 14, 1940, when he complained of dysphagia of 2 months' duration. This was accompanied by lower substernal pain and hiccup. The dysphagia increased slowly until he was able to swallow only liquids. He had lost approximately 5 pounds. He had had lobar pneumonia in 1914, and again in 1920.

Physical examination disclosed an elderly man, weighing 132 pounds, heart and lungs, negative; no enlarged lymph nodes; abdomen, negative. An esophageal roentgenogram showed a small filling defect at the cardia, with marked obstruction in the lower esophagus.

He was admitted to Mt. Sinai Hospital, where esophagoscopy (Dr. R. Kramer) revealed an obstructing, ulcerated neoplasm, beginning at 40 centimeters from the incisor teeth. The biopsy specimen showed an adenocarcinoma. Aside from a mild anemia, all laboratory examinations were negative.

Operation was performed June 28, 1940, under avertin-ethylene anesthesia. Exploration of the upper abdomen through a high left rectus incision revealed the presence of a small neoplasm at the cardia, without palpable enlarged nodes. The tumor was locally operable. However, metastatic nodules were found in the liver, and the abdomen was closed. Convalescence was uneventful, and the patient was discharged. He died of his disease 2 months later.

CASE 14. I. G., female, aged 52 years, was first seen June 22, 1940. She complained of dysphagia of 8 weeks' duration. She noted that swallowed solid food seemed to stop at a point behind the ensiform cartilage and was frequently regurgitated. The dysphagia increased in severity until she was able to swallow only liquids. There was no pain. The weight loss was 10 pounds. The past, personal and family history was negative.

Physical examination disclosed a small, thin, somewhat anemic woman, weighing 90 pounds. The heart and lungs were negative. No abdominal masses were felt. Pelvic and rectal examinations were negative. The esophageal roentgenogram showed a small, irregular filling defect in the lower esophagus just above the diaphragm, with moderate obstruction.

She was admitted to Mt. Sinai Hospital, where further study showed absence of free hydrochloric acid and marked diminution of combined acid in the gastric contents. There was moderate secondary anemia. Esophagoscopy disclosed an obstructing tumor, starting at 38 centimeters from the incisor teeth. The biopsy specimen showed fragments of esophageal wall infiltrated by adenocarcinoma.

Operation was performed June 28, 1940, under avertin-ethylene anesthesia. After a preliminary transfusion, ex-



Fig. 14. Case 15. Roentgenogram of esophagus and stomach showing intrathoracic position of upper stomach and the site of the esophagogastric anastomosis.

ploration of the upper abdomen through a high left rectus incision revealed a small neoplasm at the cardia which extended upward to involve the terminal portion of the esophagus. Although the tumor was resectable, the finding of metastatic nodules in the liver rendered the condition inoperable. A Janeway gastrostomy was performed. Convalescence was uneventful, and the wound healed by first intention. The patient succumbed 3½ months later.

CASE 15. A. M., male, aged 60 years, referred by Drs. J. Pillar and L. G. Shapiro of Paterson, New Jersey, was seen May 24, 1940. He gave a rather disconnected history, but the essential symptoms were indigestion for 35 years, consisting of epigastric fullness and belching, and midepigastric pain relieved by soda and food. During the past month, epigastric distress had been more or less steady and was more severe after meals. At no time had there been any dysphagia or vomiting. The patient had lost 15 pounds during the preceding year.

Physical examination disclosed an elderly man, in fairly good condition; heart and lungs, negative; no enlarged nodes palpable; abdomen, negative; blood pressure, 118/64. The esophageal and gastric roentgenograms showed a finger-tip defect in the cardia and lower esophagus, with minimal obstruction (Fig. 12).

He was admitted to Mt. Sinai Hospital June 2, 1940. Laboratory tests revealed hemoglobin of 63 per cent; red blood cells, 3,650,000; white blood count, normal; urine, negative; Wassermann, negative. Gastric analysis showed no free hydrochloric acid, a total acid of 50, and a faint trace of blood. Esophagoscopy (Dr. R. Kramer) disclosed a friable ulceration, at 40 centimeters from incisor teeth. Biopsy specimen from edge of ulcer showed adenocarcinoma.

Preoperative preparation consisted of a transfusion of 500 cubic centimeters of whole blood, administration of sulfanilamide, a high caloric liquid intake, the correction of a mild gum infection, and cleansing irrigations of the lower esophagus.

Operation was performed June 6, 1940, under avertin-ethylene anesthesia. Exploration of the upper abdomen was made through a small rectus incision. A tumor was felt at the cardiac orifice, with extension upward into the esophagus. There were no enlarged nodes, and the liver was negative. The wound was closed with through and through steel wire sutures. The left thoracic cavity was now opened through the eighth interspace and the eighth, seventh, and sixth ribs were divided close to the spine. The esophagus was exposed and a radial incision was made in the diaphragm. The upper stomach was mobilized by division of the left gastric and gastropiploic vessels and the tumor-bearing portion of stomach and esophagus was resected (Fig. 13). An intrathoracic end-to-side esophago-gastrostomy was then performed, two layers of fine silk being used. The stomach was telescoped over the suture line and anchored to the mediastinal pleura and diaphragm. The phrenic nerve was not disturbed, but large branches of the vagus were sacrificed. An under water drainage tube was inserted through a stab wound in the subjacent intercostal space and the wound was closed—time, 2 hours and 5 minutes. During the course of the operation, a transfusion of 500 cubic centimeters was given. The pulse varied between 88 and 136. The systolic blood pressure was fairly steady at 118 millimeters mercury.

On first day after operation temperature was 104.4 degrees F; pulse, 120, respiration, 26. Nine and one half ounces of bloody fluid drained from the intercostal tube. On second day, temperature was 103 degrees F, pulse, 110, respiration, 30. Drainage from tube amounted to 3 ounces. On third day, patient's condition was excellent, temperature, 102 degrees F, pulse, 98, respiration, 26. On fourth day, temperature was 100 degrees F; pulse, 104, respiration, 26. Small sips of water were swallowed without difficulty. Thereafter the liquid intake by mouth was rapidly increased. On seventh day, the intercostal tube was removed. The operative wounds healed *per primam*. All sutures were removed.

The patient's convalescence was uneventful. The food intake was increased rapidly. By the eighteenth day, he was swallowing all types of pureed foods and finely ground meats. He was discharged from the hospital on the twenty third postoperative day.

Now, almost 5 months later, his general condition is excellent. He has gained approximately 15 pounds and eats without difficulty (Fig. 14).

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# THE PRIMING ACTION OF STILBESTROL ON THE GRAVID HUMAN UTERUS

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OUR present day knowledge of the combination of circumstances leading to the onset of labor has been logically presented, rationally analyzed, and clearly correlated by Reynolds, who thus summarizes the situation: "... there is no known single cause for the onset of labor as the numerous theories of the past and present imply. Rather, it now seems that parturition begins as a result of the gradual accelerating convergence of a number of factors, structural, humoral, nervous, nutritional and circulatory, which, at a time characteristic of each species and adapted to the morphological conditions present in each, are so associated that they lead to evacuation by the uterus of its contents" (11).

Although the exact rôle played by estrogen is still not fully understood, most observers agree that estrogen is the main sensitizing factor for uterine muscle, including that of the human (10, 12). It was on this basis that the use of estrogen was introduced into clinical obstetrical practice by Robinson, Datnow, and Jeffcoate. Using the so called "natural" estrogens (estrone, estradiol, and their benzoic acid esters), these workers reported very encouraging results in the management of missed abortion and labor and of uterine inertia developing during the course of labor. Attempts to induce abortion in the early part of pregnancy (7 to 14 weeks) were uniformly unsuccessful (12). When even relatively huge doses of the natural estrogens were used for the induction of labor, the results were not very encouraging (8, 12, 14).

In a subsequent report Jeffcoate carefully analyzed the possible rôle that estrogen may play, while he further emphasized the excellent results obtained with large amounts of the natural estrogens in the management of uterine inertia and missed labor and abortion (6).

In order to confirm and extend the original observations noted with the natural estrogens, these studies were undertaken (2). The following considerations prompted the choice of the syn-

thetic estrogen, stilbestrol. In the first place, stilbestrol retains most of its potency when administered orally (5). This method of giving the drug thus necessitated a minimum of nursing care, while the patient was not subjected to the discomfort of a series of injections. Second, stilbestrol is not inactivated by the liver (16), while estrone and estradiol are (3, 15). Third, the natural estrogens when given in oil parenterally are slowly absorbed, while stilbestrol is rapidly absorbed from the intestinal tract (4). In summarizing these factors, then, we note that the administration of stilbestrol orally leads to a rapid accumulation of highly active estrogen in the circulating blood.

While these studies were well under way (2), Peel reported that from 10 to 50 milligrams of stilbestrol produced good results in 6 of 13 cases when used for the induction of labor, while, in uterine inertia, success, in whole or in part, was observed in 63 per cent of 11 cases (9). In 3 cases of missed abortion and labor, Peel noted excellent results. Jeffcoate recently extended his observations on the management of missed abortion and labor with estrogens, including stilbestrol, reporting excellent therapeutic response (7).

## PROCEDURES AND RESULTS

Twenty-one cases were studied. These were divided into 4 groups: induction of abortion, induction of labor, missed abortion and labor, and uterine inertia. The pertinent data are outlined in Table I.

After various trials, the following routine was finally adopted. Ten to 15 milligrams of stilbestrol was given orally each hour for 10 doses, making a total of 100 to 150 milligrams of stilbestrol administered over a period of 10 hours. From 1 to 8 hours after the last dose of stilbestrol, a routine induction<sup>1</sup> was started. The time interval

<sup>1</sup>The technique of the routine induction used in this clinic is as follows: 6 a.m. castor oil, 2 ounces; 7 a.m., quinine, 10 grains; 8 a.m., hot soap suds enema; 10 a.m., posterior pituitary extract, 3 minims; 10:30 a.m., repeat same dose; 11 a.m., repeat same dose; 11:30 a.m., repeat same dose. If labor does not ensue in 7 hours, the following is done: 7 p.m., hot soap suds enema; 7:30 p.m., posterior pituitary extract, 3 minims; 8 p.m., repeat same dose; 8:30 p.m., repeat same dose, 9 p.m., repeat same dose. As soon as active labor pains begin, the posterior pituitary extract is discontinued. If labor does not begin within 48 hours by this procedure, the induction is considered as unsuccessful.

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TABLE I—RÉSUMÉ OF 21 CASES STUDIED

Group	Case	Age	Para	Preg- nant wks	Indication	Pre- vi- ous in- duc- tion	Hrs lab- or be- fore stil- bes- trol	Cer- vix	Stil- bes- trol mgm	Hrs from first dose of stilbestrol to			Actual labor hrs	Result	Comment	
										Last dose	Start of in- duc- tion	Onset of labor after				Deliv- ery
Induction of abortion	1-5	10-27	4M 1F	7-12	Constitutional	0	0	0	100- 150	10-66	11-77	No		None	Failure	Uniformly unsuccessful
	6	23	1	41	Post mature rheumatic heart disease	2	0	0	125	15	16	12 2nd pt tussin	31	11	Success	See text
	7	35	0	37	Large baby, borderline mid pelvis	2	0	0	200	10	11	16½ 3rd pt tussin	29½	13	Success	Fully dilated in 10 hrs Midpelvic arrest 3 hrs Forceps delivery. Baby weighed 8 lbs 2 oz
	8	30	0	33	Fulminating pre-eclampsia	2	plus ca- the- ters cer- vical pack	0	100	10	11	15 Quinine	16½	34½	Success	See text
Induction of labor	9	35	5	36	Progressive toxemia	1	0	1cm 1cm	1) 50 2) 150	5	6	No 21 4th pt tucin	31½	13½	Partial success	Insufficient dosage first time? Baby weighed 7 lbs
	10	31	2	33	Eclampsia	0	0	0	150	6	7	11½ 3rd pt- tucin	14	1½	Success	See text
	11	30	0	43	Toxemia post mature	0	0	0	225	50	11	26½ 2nd pt tussin	70½	3	Success	Baby weighed 7 lbs 1 oz
	12	35	3	36	Progressive toxemia	0	0	0	100	10	18	27 4th pt tucin	35	8	Success	Baby premature
	13	37	0	37	Toxemia	0	0	0	See text						Failure	See text
	14	27	2	33	Fulminating pre-eclampsia	0	0	0	120	13	19	31 Quinine	43	11	Success	Baby weighed 6 lbs 1 oz
	15	36	0	36	Pre-eclampsia eclampsia twice before	0	0	0-1 cm	1) 150 2) 150	36	48	50 1st pt tucin 47½ 3rd pt tucin	48	¾	Partial success	Pains lasted 6 hrs. First time. Second priming 3 days later. Baby weighed 5 lbs 10 oz
Missed abortion and labor	16	37	2	25	Fetal death 1 wk	1	0	0	100	10	17	24 Quinine	61	37	Success	Stenotic cervix
	17	33	9	34	Fetus dead—6 days. Severe toxemia	0	0	0	120	13	16	31½ 4th pt tucin	38	3½	Success	See text
	18	32	0	38	Fetus dead—10 days. Severe toxemia	1	0	0-1 cm	100	36			150	6	Failure	Estrogens alone insuffi- cient, oxytocics also nec- essary
Uterine inertia	19	42	6	38	Inertia Toxemia	1	36	1-2 cm	50	5			14½	50½	Doubt ful suc- cess	Pains increased in inten- sity, not frequency. Baby weighed 5 lbs 8½ oz
	20	39	0	40	Inertia	1	70	4 cm	200	10	11	15 1st pt tussin	24	94	Success	See text
	21	30	0	41	Inertia Occiput posterior	1	60	8 cm	50	2			7	69	Success	Weak pains every 15-30 min. Half hour after 50 mgms stilbestrol pains strong every 5 min. Forceps delivery. Baby weighed 7 lbs 13 oz

intervening before the beginning of the induction was very variable at first, for the effect of the estrogen alone had to be evaluated. In fact, some cases received stilbestrol alone without subsequent medication in order to ascertain if estrogen alone would precipitate the onset of labor. When a routine induction had been previously given, an interval of at least 48 to 72 hours was allowed to elapse before stilbestrol was started. If labor did not ensue after quinine, posterior pituitary extract was given. If pains were transient, the oxytocic was repeated. The maximum number of doses which was used in this series was four, except in the group in which the induction of abortion was attempted.

*Induction of abortion.* There were 5 cases in this group, 4 being multiparas. They were from 7 to 12 weeks pregnant. A Friedman test in each was positive. The indication for interrupting pregnancy was constitutional, not local, in each instance. Stilbestrol was administered orally in divided amounts, the total dosage ranging from 100 to 250 milligrams over a period of 12 to 72 hours. This was followed by a complete induction including pituitrin, one patient receiving an additional course of ergonovine, 1/320 grain, three times a day for 3 days. In 2, uterine cramps occurred as though menstruation was imminent, after pituitrin was given. In a third patient, slight and transient vaginal spotting resulted. In the primigravida, the nausea that was already present, was aggravated by stilbestrol. This was allayed to a great extent by the simultaneous administration of bile salts (2).

*In each case, the attempt to produce an early abortion proved entirely unsuccessful, even though massive doses of stilbestrol, combined with potent oxytocics, were used.*

*Induction of labor.* Ten cases were included in this group. In 7, the indication for terminating pregnancy was a progressive or fulminating toxemia unresponsive to conservative measures. In the 3 others, there was one case each of eclampsia, post maturity associated with rheumatic heart disease, and an elderly primigravida with a large baby and a border line mid-pelvis.

As a rule, the procedure outlined was followed. The exceptions are detailed in Table I. In 2 patients, Cases 6 and 7, 2 previous complete inductions 48 hours apart failed to institute labor. In 2 others, Cases 8 and 9, a previous induction, including the use of extraovular catheters and cervical packing in 1, Case 8, did not precipitate labor. In each of these 4 cases, labor ensued only after first priming with stilbestrol and then using oxytocics. Since the claim might be made that

the previous induction had served to sensitize the uterus in some way, the routine induction was omitted in other cases. In some, the toxemia was so severe that it was deemed wiser to help insure a successful induction by first priming with stilbestrol.

In only 1 instance, Case 13, did the uterus fail to respond to oxytocics after the preliminary administration of stilbestrol. The results in the other 9 cases were considered excellent, even though 2, Cases 9 and 15, required a second course of stilbestrol.

The following cases are presented to illustrate the method of approach.

CASE 6. J. B., 118605, aged 23 years, white, secundigravida, primipara, was admitted to the antenatal cardiac ward because of an attack of acute rheumatic fever with cardiac and joint manifestations during her fifth month of gestation. After almost 3 months of bed rest, she was vastly improved clinically except for a mild tachycardia of around 110. She was closely observed until term. After she was past due for 1 week, a medical induction without pituitrin was given with no results. A few days later, a complete induction with pituitrin was given with no effect. Two days later this was repeated with the same negative results. The cervix was still moderately firm and undilated. Three days later, when she was 15 days overdue, she received 25 milligrams of stilbestrol for 3 doses at 7, 8, and 9 p.m. The next morning she received 10 milligrams of stilbestrol every hour for 5 doses, making a total dosage of 125 milligrams. This was followed by a routine induction. After the first dose of pituitrin she began to have irregular contractions which seemed to die out. Five hours later she received a second dose of pituitrin, irregular contractions reappeared, but soon became strong and regular. She delivered spontaneously 6 hours later of a normal female child weighing 9 pounds, 3 ounces (4,167 grams). Total labor, then, counting from the first pain was 11 hours, even though active labor lasted only 6 hours. Lactation set in normally and was fully adequate.

CASE 8. V. G., 116,251, aged 20 years, Porto Rican, secundigravida, nullipara, was admitted to the toxemia ward because of epigastric distress, marked blurring of vision, and ankle edema. Her past history revealed that she had had eclampsia 11 months before.

She was 8 months pregnant. Blood pressure on admission was 215/160. Urinalysis disclosed 4 plus albumin and many hyaline and granular casts. Examination of the eye grounds showed signs of recent hemorrhage, papilledema, cotton wool exudate, and a definite narrowing of the arteries. The fetal heart was regular in rate and rhythm.

A modified Strogonoff regimen was instituted. Blood chemistry studies showed a urea-nitrogen of 34.7, creatinine of 2.0; sugar of 0.4; uric acid of 8.3. Two rubber catheters were introduced extraovularly, the cervical canal was tightly packed and a routine induction started, pitocin being used. She failed to go into labor. Temperature rose to 102 degrees. At this time the fetal heart sounds disappeared. Two days later, the urea-nitrogen was 53.5; creatinine, 3.1; and uric acid, 8.3. She was then given 10 milligrams of stilbestrol orally every hour for 10 hours, making a total dosage of 100 milligrams. This was followed by castor oil, a hot enema and 10 grains of quinine. Following the latter she went into active labor. In 3 hours and 10 minutes she delivered a stillborn infant. On the next day, the blood chemistry studies revealed essentially no



change, urea-nitrogen being 54.3 and creatinine 3.1. Five days later her uric acid fell to 5.2, creatinine to 2.0, and urea-nitrogen to 42.9. Her postpartum course was very hectic and septic. The cause was finally determined to be malaria, several positive smears being secured.

CASE 10 C.B., 120, 130, white, aged 34 years, trigravida, secundipara, was admitted to the toxemia ward at 32 weeks of gestation because of a fulminating toxemia. Two weeks before admission, her blood pressure, which had been normal, rose to 140/90. Since then in spite of careful medical care and strong conservative therapy, her blood pressure steadily increased, and was 220/110 on admission. At this time she complained of marked epigastric distress and persistent pain over the gall bladder region. Edema was 3 plus while urinalysis showed a 4 plus albuminuria with many granular casts. Benzidine test for blood was strongly positive. Ten minutes after admission to the ward, she had an eclamptic convulsion. She was heavily sedated receiving enough morphine to reduce her respiration to 10 to 12 per minute. Blood chemistry studies at this time showed sugar, 87, urea-nitrogen, 44.1, uric acid 9.2, chlorides, 600, total cholesterol, 230, cholesterol esters, 147, creatinine, 2.4, carbon dioxide volumes per cent, 52.7. The fetal heart sounds disappeared 12 hours after admission.

After 24 hours of conservative therapy on a modified Stroganoff regimen, she seemed somewhat better. Since her prognosis was very grave, it was felt best to deliver her as rapidly as possible. Cervix was undilated, moderately firm in consistency. Accordingly, the next morning, she received 25 milligrams of stilbestrol every hour for 6 hours, making a total of 150 milligrams. One hour after the last dose, the routine induction was started, pitocin being used. She went into labor after the third dose and spontaneously delivered a stillborn child 2 hours and 20 minutes later. The next day her urine showed a 2 plus albumin. Forty-eight hours later just a trace was found. The blood uric acid had fallen to 8.5; the other values remaining unchanged. A week later, uric acid was 3.5, urea nitrogen, 22.4. The other findings were normal. She was discharged well in 3 weeks.

CASE 13 R.B., 115, 161, negress, aged 37 years, secundipara, nullipara, was admitted to the hospital for observation because of a sudden rise in blood pressure to 160/90 and 1 plus albuminuria which developed during antipyloric therapy with neosphenamine. She was 34 weeks pregnant. On conservative therapy she improved. When she was 37 weeks pregnant the following observations were recorded: Cervix was long, firm, undilated. She received 50 milligrams of stilbestrol daily in 10 milligram doses for 3 days, making a total dosage of 150 milligrams. Labor did not ensue. On the fourth day she received a routine induction. After the third dose of pitocin she began to have active pains. These lasted for 5 hours, then died out.

During the course of the next 2 days she received 150 milligrams of stilbestrol followed by another routine induction. After the third dose of pitocin, she began to have active pains. These lasted for only 6 hours.

After a 24 hour rest, at the suggestion of Dr. Leo Wilson, she received 100 milligrams of anhydro-oxy progesterone for 3 days, making a total dosage of 300 milligrams. Labor did not ensue. On the fourth day, after she had received 2 doses of pitocin, she apparently had a few mild contractions during the course of an hour.

Two days later it was decided to combine stilbestrol and anhydro-oxy progesterone. Accordingly, she received 50 milligrams of stilbestrol during the course of one day, 100 milligrams of pregnenolone on the second day, and a routine induction on the third day. After the third dose of pitocin she had strong pains which lasted for one hour.

Three days later, she had a normal spontaneous delivery after a total labor of 6 1/2 hours. The baby weighed 7 pounds, 2 ounces (3,230 grams). Furthermore, lactation was normal.

**Missed abortion and labor.** There were 3 cases in this group, 2 of missed labor associated with progressive toxemia and the third a case of missed abortion (Cases 16, 17, 18). Results were excellent in Cases 16 and 17. In Case 18, one of missed labor, stilbestrol alone, given without subsequent oxytocics, was without effect. The results obtained in this group are similar to the ones secured with the natural estrogens (6, 12) and stilbestrol (7, 9).

The following case indicates the successful priming action of stilbestrol in an instance of missed labor.

CASE 17 G.M., 114, 436, aged 35 years, decigravida nonipara, was admitted to the toxemia ward 6 weeks before term because her blood pressure had risen to 176/104 while urinalysis revealed a 4 plus albuminuria and occasional casts. The patient complained of marked nausea, vomiting, and severe headaches. She had not felt "fetus" for over a week. Blood chemistry studies were within normal limits except for a serum protein of 4.93. Peripheral edema was marked. Fetal heart sounds were not heard.

On conservative therapy she failed to respond. It was felt that evacuation of the uterus was imperative. Cervix was fairly firm, and was a finger tip dilated. Accordingly, she received 10 milligrams of stilbestrol every hour for 12 doses, making a total dosage of 120 milligrams of stilbestrol. She failed to go into labor in 14 hours. A routine induction was then started. After the fourth dose of pitocin, she went into active labor, delivering a stillborn macerated fetus 3 hours and 25 minutes later.

**Uterine inertia.** Three cases of uterine inertia were studied. The result in 2, Cases 20 and 21, was considered successful. In the third, Case 19, the result was good, but was classified as doubtful for the pains increased in intensity but not in frequency. The results obtained compare favorably with those secured with the natural estrogens (6, 12) and with stilbestrol (9).

The following case is presented in detail to illustrate the method of approach.

CASE 20 (The author is indebted to Dr. Ramon Basora for the details of this case) E.S., white, aged 19 years, secundigravida, nullipara, 1 miscarriage. Pregnancy was uneventful until her blood pressure rose to 140/90 3 days after her expected date of confinement following which she went into labor, pains occurring at 15 to 20 minute intervals, being weak in intensity. These continued for 3 days the cervix dilating to 3 to 4 centimeters. Pains then died out. She was given a routine induction following which she went into labor, pains occurring at 15 to 20 minute intervals, being weak in intensity. These continued for 3 days the cervix dilating to 3 to 4 centimeters. Pains then died out. The next morning she was given 10 milligrams of stilbestrol every hour for 10 doses making a total dosage of 100 milligrams. Another induction was started and after the first dose of pitocin she went into very active labor and was delivered of a normal female child by prophylactic low forceps a little less than 9 hours later.

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## ANALYSIS OF RESULTS

The results obtained in cases of uterine inertia and missed abortion and labor are similar to those reported elsewhere both for the natural estrogens and for stilbestrol. Attempts to induce abortion with stilbestrol in the early part of pregnancy were as uniformly unsuccessful as those noted with natural estrogens. Why the uterus should fail to respond in the early weeks of pregnancy still is beyond the ken of our present day knowledge.

After the first half of gestation, however, the uterus apparently becomes responsive to potent oxytocics after preliminary priming with sufficient amounts of estrogen. To this may be ascribed the favorable results secured in the induction of labor. The results obtained with stilbestrol, moreover, seem to be somewhat better than those obtained with the so called natural estrogens—estradiol and estrone (8, 12, 14). In discussing the use of estradiol and estrone for the induction of labor, Robinson, Datnow, and Jeffcoate stated that the administration of these estrogens near term may bring on labor, but was not reliable, whereas for cases where rapid delivery was essential, estrogen was unsuitable (3). These statements must be qualified by the following considerations. In the first place, the natural estrogens administered parenterally in oil, a factor hindering rapid absorption. Second, the natural estrogens are inactivated by the liver (3, 15), while stilbestrol is not (16). Moreover, stilbestrol is readily absorbed from the intestinal tract. In short, the metabolism of stilbestrol in the circulating blood is rapidly attained. By using large doses over a relatively short period of time, a successful therapeutic result is further ensured. The results obtained in this series appear to offer valid evidence supporting these statements.

Analysis of the data in Table I apparently demonstrates that the estrogen, stilbestrol, alone, regardless of dosage (up to 225 mgms.) or time (3 days), did not initiate labor. Furthermore, 4 patients one or more inductions, including the use of potent oxytocic posterior pituitary extracts, had been unsuccessful. In short, the use of estrogen alone or the use of oxytocics was used in sufficient dosage to sensitize the uterus to the subsequent action of oxytocics that labor ensued. Moreover, it should be noted that labor practically always set in within a very short time after the administration of oxytocics was begun. This phenomenon might be called a one-two reaction (estrogen-oxytocic).

All in all, these data seem to show that a successful and rapid induction of labor in the last trimester of pregnancy may be insured by the preliminary priming of the uterus with 100 to 150 milligrams of oral stilbestrol to the subsequent action of potent oxytocics.

A word may be said about the so called "toxic" effects of stilbestrol noted especially in the menopausal patient (13). The most frequent side effect seemed to be nausea and vomiting. Previous studies in this clinic had demonstrated that the puerperal patient could easily ingest from 250 milligrams of stilbestrol daily to 1500 milligrams weekly (1). Careful blood and urine studies had failed to disclose any so called "toxic" effects. Consequently, it was felt that stilbestrol was a safe substance to administer to the pregnant patient, even though evident cardiovascular, renal or hepatic damage might be present. In 15 of the cases in this series, some evidence of toxemia was found, yet no harmful effects could be ascertained even by extremely critical observers. Two patients experienced mild nausea, which was relieved by bile salts. A third one, who vomited after a meal containing cabbage, experienced difficulty whatsoever 2 days later when she received a similar amount of stilbestrol.

The duration of labor in the successful cases seemed, as a rule, to be somewhat less than normal. It should be noted that the duration of labor has been calculated from the time of the first pain, not from the time pains become strong and regular. In the vast majority the labor progressed very smoothly. No adverse effects were noted in the third stage of labor either with separation of the placenta or postpartum bleeding. Careful pediatric check up failed to note any effects upon the babies.

There was one case of puerperal morbidity, Case 8, which was found to be caused by malaria. In those mothers who nursed their babies no ill effect was observed upon subsequent lactation. The initiation of milk secretion was not delayed (1). In the toxemia patients the elevated blood pressure seemed to be unaffected by stilbestrol.

## SUMMARY

1. Attempts to induce early abortion with stilbestrol were uniformly unsuccessful in 5 cases. Stilbestrol in dosages from 100 to 250 milligrams orally failed to prime the gravid uterus of the first trimester of pregnancy to the subsequent action of potent oxytocics.
2. For the induction of labor in the last trimester of pregnancy, stilbestrol, in oral dosages averaging 100 to 150 milligrams, appeared to be

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an excellent priming agent for the subsequent action of oxytocics on the gravid uterus. The result was considered successful in 9 cases, 90 per cent, although in 2 of these a second priming with stilbestrol was necessary. Stilbestrol alone was ineffectual. It was only when this estrogen was followed by the use of potent oxytocics that labor ensued. These results are merely suggestive and far from conclusive.

3. In one case of missed abortion and one of missed labor, stilbestrol successfully primed the uterus to the subsequent action of oxytocics. In a second case of missed labor, the use of stilbestrol alone, without being followed by oxytocics, proved unsuccessful in precipitating labor.

4. In 3 instances of uterine inertia, a good result was apparently secured in 2, while in the third, the effectiveness of stilbestrol *per se* seemed questionable, even though the result appeared to be good.

5. The pregnant patient, especially in the last trimester of pregnancy, is very tolerant of large doses of oral stilbestrol, even though severe grades of toxemia may be present.

6. No adverse effects were observed upon the third stage of labor, the babies, the post-

partum morbidity, the lochia, or upon the subsequent lactation.

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# THE EFFECT OF COOLING TRAUMATIZED AND POTENTIALLY INFECTED LIMBS

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FOR centuries the beneficial effects of heat and cold in the treatment of infection has been appreciated. But as Brooks and Duncan have pointed out, the outstanding fact is the paucity of investigative knowledge relative to the effects of heat and cold on tissue.

Allen has done both experimental and clinical study on the effect of cooling limbs rendered ischemic by tourniquet, by ligating great vessels, or by vascular accident. Allen states: "Theoretically, at least, the following possible uses of cooling an extremity may be suggested."

1. In embolectomy. With prompt cooling of limbs the time limit in which embolectomy can be performed can be lengthened beyond 4 hours. Allen bases this statement on the fact that he has shown experimentally that cooling limbs subjected to local asphyxia by tourniquet or by ligating great vessels greatly prolongs the time a tourniquet can be left on a limb with resultant recovery when the constrictor is removed.

2. In diabetic and arteriosclerotic gangrene.
3. In emergency surgery. "Theoretically this plan of cooling a limb and applying a tourniquet can be recommended more positively for emergency purposes. Occasionally there are accidents in isolated localities and on a larger scale there are military emergencies when anesthetics may be lacking or surgical care may be delayed. If ice is available the tourniquet and refrigeration can be applied by anybody of reasonable intelligence. Hemorrhage and pain are thus stopped and both local tissue damage and the systemic shock which prolonged ligation at ordinary temperatures produces are abolished. Theoretically a limb might be preserved in ice or ice water for twenty-four hours or more if the ligation is not too high but it is safer to limit the time to five or six hours." This statement refers to limbs in which survival of the part is to be sought.

I first became acquainted with the application of Allen's work about 18 months ago when I had an opportunity to observe the work being done on the Fifth Surgical Service at the Boston City Hospital. At that time the following method of treating gangrene of the foot in the elderly or poor risk patient was started:

From the West Suburban Hospital, Oak Park.

The limb was surrounded with shaved ice up to the elected site of proposed amputation in the thigh. Soon after icing, all pain would disappear from the limb. Twenty-four hours after the application of the ice, a tourniquet would be placed tightly about the thigh just below the site of proposed amputation. Because absorption of toxins was prevented by this treatment, the patient would begin to improve. In 4 to 5 days his condition would be such that amputation could be done. The tourniquet would then be removed and the amputation would be done through the tourniquet site with no anesthetic except that provided by the pressure produced by the tourniquet. I watched an amputation in one of these cases and it appeared to be absolutely painless and was practically bloodless.

Allen (1) states: "The only right way to present a new practical proposal is on the basis of a sufficient series of case records for demonstration, and the lack of such is regretted. A possible use of refrigeration in nondiabetic surgery for reducing shock in extensive injuries and operations involving the lower limbs and pelvis must also be left as a mere theoretical suggestion."

The following case is presented because it is believed that beneficial effects, both general and local, were obtained by the application of Allen's principles to a severe traumatic injury; also to bring forth the fact that cooling was used not to preserve a portion of a limb but to prevent the development and progress of bacterial infection and invasion in heavily contaminated and potentially infected wounds.

The morning of November 30, 1940, I was called to see a man aged 50 years, who 1 hour previously had been run over by a railroad train which had amputated his left leg just above the knee and his right leg through the knee joint. The man was lying on the floor of the emergency room when I first saw him.

The house surgeon had applied tourniquets about the thighs. The man was bled out and was in profound shock. His blood pressure was 30/0. He was receiving 1500 cubic centimeters of gum acacia through the veins of both arms. As soon as possible whole blood was given because it was felt it would be more beneficial than blood serum. The tourniquets were released and all bleeding points were seized with hemostats which were left in place. The tourniquets were left around the thighs in case they were needed. The stumps were wrapped in gauze soaked in a solution of sulfanilamide.

Two hours later the patient's blood pressure was 40/0. Eight hours after injury his blood pressure was 50/10.

The day of the accident was slushy and because of the sudden application of the train's brakes, the undercarriage of the cars had rained snow, mud, and sand over the limbs. This material was ground up and mixed with clothing, huge flaps of skin, muscle, and bone. The ends of the stumps were ragged and extensively macerated.

Ten hours after injury the patient complained of pain in the left chest. He was irrational and was tossing from side to side complaining of pain in his feet and legs. An electrocardiogram showed sinus tachycardia. His blood pressure remained about the same.

Twenty hours after injury a pronounced foul odor was emanating from the stumps. Large doses of morphine were needed to control him. He was coughing. He was irrational. His blood pressure had shown no rise. A consultant confirmed the diagnosis of pneumonia and sulfapyridine was substituted for the sulfanilamide he had been getting. He still received neoprontol. His temperature was 101.4 degrees by axilla.

It was evident that nothing at this time could be done for the patient's lower extremities. The gauze was removed from the stumps and they were completely enclosed in shaved ice to 2 inches above the extent of tissue damage. No tourniquets were applied. Within 1 hour following the application of the ice all pain ceased in the lower limbs. Soon the foul odor from the stumps vanished. The patient soon became quite rational and it was possible to take his temperature by mouth. The icing profoundly affected his temperature because it fell to 97.2 degrees by mouth. Heat blankets were applied over the patient's body and his temperature again rose to around 101.0 degrees by mouth. Supportive treatment was given including blood. He was given three successive prophylactic doses of combined sera.

On Monday afternoon, December 2, 58 hours after injury the patient's condition had markedly improved. Blood pressure was 110/60. Fever was 101 degrees by mouth. The pneumonia was not progressing. At this time the patient was taken to the operating room and under ethylene anesthesia both lower extremities were elevated, high tourniquets were applied, and a simultaneous bilateral amputation was done. On the left side the site was through the mid-thigh and on the right side the site was through the lower third of the thigh. A 'fish mouth' type of incision was used. The muscle jumped and retracted smartly. The flaps were allowed to fall together. Soft rubber drains were inserted and a few loose silkworm sutures were used to gently approximate the flaps. There was no redness, induration, or ecchymosis of either thigh at or below the site of amputation. During operation his blood pressure fell from 110 to 105. He was transfused on the operating table.

The day following operation the patient broke into a profuse sweat. His fever dropped by crisis to normal. His chest condition rapidly resolved. Since that time the patient's recovery has been uneventful. His fever never exceeded 100 degrees by mouth and after the sixth post-operative day it has been normal. Five days after surgery the patient was sitting up in bed reading a paper and smoking his pipe. The stumps were healing kindly with no signs of induration, infection, or slough of skin or other tissue. Drainage from both stumps was diminishing and at the end of 6 weeks both stumps were practically healed.

The appearance of the amputated parts was interesting. They were cold and firm. There was no gross evidence of infection or inflammation. The muscle was red and healthy looking. The fascia glistened. There were no blood clots. This was probably due to the washing achieved by the melting ice. The blood was red and fresh looking. The mud

and sand were moist and looked as if of the day of the accident. The particles of sand stood out in bold relief on the surface of the tissue with no signs of sticking to the tissue as is so often seen in wounds that are softened by disintegration of tissue. The subcutaneous fat was firm. There was no odor except from a few soft, bluish white tags of skin which had not been included in the ice.

A case has been presented of traumatic amputation in which ice was used to surround the members in order to prevent the advance of bacterial infection. The purpose of this was to obtain time in which the patient's general condition could be improved sufficiently to permit major surgery. In this case 58 hours elapsed between the time of accident and the surgical amputation of both limbs through the thigh.

This case does not permit one to say whether the oral sulfapyridine, the intramuscular neoprontol, the local sulfanilamide, or the local icing was the determining factor in the result. The lack of cultures taken from the wounds limits effective discussion. It would seem, however, that icing did stop local pain, did materially aid the patient in combating shock, and did stop all odors emanating from the stumps. The patient's improvement was remarkable following the application of the ice. The pieces of skin not included in the ice were gangrenous while equally detached pieces of skin that were included in the ice were well preserved. Physiologically and bacteriologically the procedure would seem to be sound.

If upon continued investigation these findings are confirmed, the method advocated by Allen of cooling limbs might find wide application in severe wounds in both civil and military life. This cooling might be effected by ice or gas. It would be of use not only in extremities that might be saved but it would be of value in holding infection in abeyance in hopelessly traumatized limbs or parts in those cases in which surgical aid is not immediately forthcoming either because of the patient or because of the circumstances under which the accident occurred.

Undoubtedly ice has been used for the purpose reported here but the writer was unable to find reference to any such case. With this in mind it is hoped others will try the method to see if the principles advocated by Allen and applied here are substantiated by extensive clinical experience.

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# EDITORIALS

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AUGUST, 1941

### THICK SPLIT SKIN GRAFTS IN THE REPAIR OF BURNS

WHEN the full thickness of the skin is destroyed by a burn over a large area, an open wound results, and, unless there is early replacement of the lost skin, healing will occur by contraction of adjacent tissue and by "scar" epithelium, or permanent healing may never occur.

Almost any treatment that promises as little work as possible is apt to become popular; but, so far, no application has been found that will produce normal skin and, when it is claimed that a certain preparation will insure complete healing without scarring, it apparently is not realized how healing occurs in superficial and in full thickness losses of skin.

If there is rapid healing and return to function following a burn without much scarring or deformity, this simply means that the full thickness of the skin has not been lost, and that regeneration has occurred from the deep glands in the derma, much the same as occurs in the donor site of a thick split graft.

It has been observed that these struggling cells are easily killed by chemical, bacterial, or mechanical trauma. Therefore, it appears that cleanliness, protection, and the avoidance of strong chemicals will best promote this type of healing, and these objects of treatment seem to have stood the test of time.

*The local care of open wounds* has for its object the cleaning up of the areas as quickly as possible, so that the lost surface may be restored with skin grafts before contractures have occurred and before debilitation and pain have developed beyond control. Soap and water cleansing and surgical drainage accomplished by saline dressings or saline baths usually suffice, but antiseptics, Dakin's solution, or sulfanilamide may be thought necessary.

A fundamental of dressing all raw wounds is that old linen, or very fine mesh gauze be placed next to the surface so that granulations will not grow up through the coarse meshes of overlying gauze, stick, and cause pain. When cellulitis is controlled, grease dressings on fine gauze or linen can be used.

A firm pressure or elastic dressing may be of great advantage, and discolored, edematous granulations may be flattened out into a firm, bright red surface without chemicals or without cutting them away.

The continual saline bath may have the important result that most secondary contractures will be straightened out by the voluntary effort of the patient without the use of traction or restraints. Many patients are extremely grateful for the bath and realize their first comfort in it, and it has occasionally been a life-saving measure. If there is any unfavorable reaction to the bath, it is omitted.

It seems impossible to sterilize large open areas, but careful evaluation of the general condition and of the gross appearance of the granulations and surrounding tissues usually suffices for the determination of the time for operation, and many deep burns are ready for grafting in 3 weeks' time.

The general condition of the patient is directly reflected in the wounds and, of course, should be considered primarily in all instances. Gentleness in all manipulations is always an essential of care.

A graft of from one-half to three-fourths of the thickness of the whole skin is perhaps the most useful in making repairs of raw surfaces. This could be designated as a "thick Ollier-Thiersch" or as a "thick split-graft." (The original Ollier-Thiersch graft was described as being cut just through the papillary layer of the epidermis which makes it very thin without any derma; however, the thin pad of derma happens to be a most important part of a skin graft.)

When large areas are to be covered, it is necessary to obtain large thick grafts without cutting entirely through the derma so that healing of the donor site can occur rapidly without leaving any further defect. The deep glands left behind in the derma of the donor site "de-differentiate" into squamous epithelium and cover the surface in from six to eight days. This can be shown microscopically and is a very interesting study in wound healing, and might be considered as a reverse of the process of carcinoma formation. As many as five "crops" of skin have been cut from the same area and as little as nineteen days have been required for the production of a new surface suitable to supply another crop. There must be careful protection of the donor sites.

The most necessary equipment in obtaining split skin grafts is a very sharp, long knife of the amputation variety. Large grafts may be

cut rapidly, and the larger they are the more easily they may be applied; grafts up to eighteen by five inches may be obtained from suitable thighs. With some practice the thickness can be easily graduated with free hand-cutting; one should realize that the thickness of the graft should depend on the relative full thickness of the skin of the area. This thickness varies greatly in different parts of the body and in different patients, so that a set thickness cannot be described for this graft. The essential is that it be cut thick but not too thick to prevent the donor site from healing promptly.

With mechanical aids such as the dermatome, the suction retractor, or by elevation of the skin with large tenacula, fairly large grafts may be cut even from the abdomen. But patented equipment does not cut the graft and care has to be exercised in their use not to cut through the derma.

These grafts are applied to the prepared area, and held at about normal skin tension with No. 000 silk sutures all around and with multiple mattressing sutures over the surface. In suitable areas the grafts may be spread out and then "snubbed" in place with a sterile fine mesh roller bandage.

Either saline or grease fine mesh gauze dressings are used according to the degree of contamination thought to be present, and pressure is obtained over the area with mechanic's cotton waste or marine sponges bound on firmly with heavy gauze rolls. The application of pressure to the dressings is a fundamental as important as any other operative step.

Many methods of cutting split grafts have been described and different terms applied to the graft. If the full thickness of the skin is not taken, then the skin necessarily has been split in two and the graft is at least anatomically a "split" graft. To have a new type of

## EDITORIALS

skin graft would require a new type of skin, but, as new authors realize how utilizable the split graft really is, enthusiastic reports are made with new terminology.

Full thickness grafts are not put over large raw surfaces because the size required is prohibitive, and the take of a full thickness dissected graft is not as certain in contaminated fields as that of the split graft. This graft is used extensively in healed deformities in which a clean operation can be done, mainly on exposed surfaces, and the healing seems to give a better chance of immediate return of the area to normal. Even in these grafts, pigmentation may be troublesome and require the use of cosmetics.

There is a large field of usefulness involved in this work and large room for improvement, such as simplification of effort, study of the effect of local refrigeration, and the possibility of getting the homografts to survive. At the present time, with careful removal of the grafts so that prompt healing of the donor site occurs, most patients can supply enough skin for their repair. As many as five crops have been taken from the same area, 220 square inches have been transferred at one time and a total of 600 square inches has been grafted in a single patient. The laborious use of full thickness grafts and more tedious use of pedicle flaps in many instances can be avoided.

JAMES BARRETT BROWN.

## A FORUM ON FUNDAMENTAL SURGICAL PROBLEMS

**I**N the program for the next meeting of the American College of Surgeons at Boston, November 3 to 7, 1941, an experiment will be tried. On three mornings a series of brief presentations of advances in surgery will be made by representatives of various university departments of surgery. In general the repre-

sentatives will be the younger men, many of them too young to fulfill the age requirement for fellowship in the College. This innovation in its program will be under the direction of Dr. Owen H. Wangenstein of the University of Minnesota.

The College recognizes a need long felt by many to give those beginning productive careers in surgery an opportunity to present the results of their own research activities. Although it is generally realized, as Osler pointed out long ago, that the most important original work is the product of the young man, but little opportunity has been given him to present his ideas and work before the representative surgical bodies of this country. In the national societies one of the requirements for fellowship is that the candidate have reached a certain age before he can become a member or appear on the program of the Society. Somewhat in protest against the restrictions placed upon the younger, productive surgeon, the last two years have witnessed the creation of two new organizations which are primarily for the younger men: the Society of University Surgeons and the Central Surgical Association.

In the creation of the forum on fundamental surgical problems the College believes that a dual opportunity is afforded to carry out its original purpose; it is hoped that this innovation will not only fulfill the need of giving the younger surgical investigators an audience but that it will also serve as a means of acquainting the older surgeons with the newer developments. Surgery has moved on from the time when it was based only on anatomy and pathology. Physiology, chemistry and physics are now important sources of inspiration for it. If he wishes to be in the forefront of his profession, the modern surgeon must be versed in the applications of what may seem to be only distantly related sciences.



Facsimile of a letter of James Syme, Scotch surgeon known for his description of an operation for amputation at the ankle joint

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## REVIEWS OF NEW BOOKS

THE general pattern of the first edition in 1918 is followed in the ninth edition of Macleod's *Physiology and Biochemistry in Modern Medicine*.<sup>1</sup> In later editions the proportion of biochemistry was reduced and the title was correspondingly changed. The first edition was mainly the work of the late J. J. R. Macleod; the present edition is the work of Bard, as editor and part author, and of nine collaborating specialists.

The intention has been to treat a wide range of topics in physiology in a fundamental, detailed, and critical way: to avoid, on the one hand, the historical approach, exposition of laboratory method, and compact treatment desirable in an introductory textbook and, on the other hand, the "predigested knowledge suitable for immediate bedside application" desirable in practical work for quick reference. The book is not intended as a survey for beginners, nor does it set out to cover all aspects and divisions of human physiology. The outstanding omission, as in former editions, is the physical physiology of reproduction; by a paradox the authors include the chemical aspects of this subject.

The book should be extremely valuable to anyone who undertakes laboratory or clinical research on problems presenting physiological aspects. Its value from this standpoint is enhanced by a remarkable bibliography of more than 2200 references, an excellent key for existing physiological literature. It will also make useful collateral reading for medical students and will interest physicians endeavoring to keep up with the times.

FREDERIC T. JUNG.

THE fact that the splendid volume, *Anus, Rectum, Sigmoid Colon* by Bacon,<sup>2</sup> appears in a second edition so soon after its initial publication (17 months) speaks for its wide and ready acceptance by those who are interested in proctology. The book is definitely encyclopedic in form, encompassing as it does the entire field of rectal surgery and allied subjects. There is an outline preceding and a most complete and up-to-date bibliography following each chapter. The work is well organized for quick reference.

Surgical anatomy, methods of examination, aids in diagnosis, anesthesia, and analgesia are taken up in the first 100 pages. In the remaining 747 pages, the author presents a systematic and thorough discussion of all the pathological processes affecting the peri-

anal area, anus, rectum, and sigmoid colon. The so called minor rectal ailments receive as much attention as do the major problems.

Detailed step by step directions are given for the treatment of such common anal conditions as fissure, cryptitis, hemorrhoids, abscess, fistula, and pruritis ani. Nearly a third of the book is devoted to benign and malignant tumors of the rectum. The surgical technique of Miles, Gabriel, Jones, Lahey, Rankin, Lockhart-Mummery, Babcock, Coffey, Bickham, and Mikulicz are described and the applicability of each to the various types and locations of rectal carcinoma is given.

This second edition includes new operative procedures for rectal prolapse and hemorrhoids, together with various means of avoiding postoperative pain. There is a description of Devine's defunctioning colostomy. Included is a discussion of the author's recent work on extrarectal metastatic growths from upper abdominal malignancy, which are often mistaken for primary rectal carcinoma. The surgical treatment of supravertebra abscess, both of the retro-rectal and pelvirectal fossae, is given. The treatment of chronic ulcerative proctosigmoiditis and the sequelae of lymphogranuloma inguinale with sulfanilamide is described.

In order to ease the reader in the selection of the procedure of choice, summaries of treatment have been placed at the end of many chapters.

Four hundred eighty-seven illustrations and clinical photographs, as well as numerous "differential diagnosis charts," are used to enhance the work, and are uniformly good.

The book is written in a concise, direct, and readable manner. It is highly recommended as a guide for the general practitioner or surgeon and as a book of reference for the specialist.

THOMAS J. MERAR.

THE 910 page book *Emergency Surgery* by Hamilton Bailey<sup>3</sup> contains some 930 illustrations, many in color. It covers in encyclopedic style most of the surgical conditions which may be considered as emergencies as well as many which can hardly be classed as such. The book has all of the advantages to be gained from a personalized style of presentation.

Although of value to the surgeon of broad experience its chief use will be that of a handy reference for the occasional operator confronted with an emergency case. Like all textbooks it is somewhat

<sup>1</sup>MACLEOD'S PHYSIOLOGY IN MODERN MEDICINE. Edited by Philip Bard, et al. 9th ed. St. Louis: The C. V. Mosby Co., 1941.  
<sup>2</sup>ANUS, RECTUM, SIGMOID COLON; DIAGNOSIS AND TREATMENT. By Harry Ellicott Bacon, B.S., M.D., F.A.C.S., F.A.P.S. Philadelphia, Montreal, and London: J. B. Lippincott Co., 1941.  
<sup>3</sup>EMERGENCY SURGERY. By Hamilton Bailey, F.R.C.S. (Eng.). 4th ed. Baltimore: The Williams & Wilkins Co., 1940.

out of date by the time it reaches the press. The small amount of space devoted to the use of heparin in vascular surgery is an example of this type of defect.

THOMAS DOUGLASS

THIS year marks the fortieth anniversary of the Year Book series and the ninth of the *Year Book of Radiology*.<sup>1</sup> The editors have co-operated in celebrating this anniversary year by contributing previously unpublished papers on subjects with which they have been prominently identified. Dr. Waters' paper deals with preoperative irradiation of renal tumors while Dr. Kaplan reports on his rich experience with the treatment of amenorrhea and sterility. A very readable preface, "The Story of the Year Book of Radiology" by the publishers, adds considerable interest to the volume.

As in previous years this edition covers the progress of radiology during the past year in a concise yet adequate manner. The selection of the material to be reviewed by the editors reflects the value of their wide experience and sound judgment. It is of interest to note that there has not been such a marked decrease in available contributions from abroad as might be expected. Whereas the diagnostic section of the 1939 edition consisted of approximately 45 per cent of foreign articles, in this edition slightly less than 35 per cent of the material came from foreign sources. Dr. Kaplan, however, mentions the effect of the international situation as reflected by the value of the articles dealing with radiotherapeutics published abroad. The safeguarding of radium in the countries at war has become a problem. Provisions have been made in some countries for underground storage to prevent loss and scattering of radium following explosive destruction.

A review of this edition impresses one with the continued growth and expansion of the science of radiology. It would be superfluous to attempt to select particular papers as outstanding. Every page contains items of interest and importance. The *Year Book of Radiology* has proved its value during the past years. The same excellent qualities are preserved in this edition. The reviewer finds it indispensable in his work and ventures to say that this is the feeling of the great majority of radiologists. It is recommended without reservation not only to the radiologist but to any physician who is interested in acquainting himself with the recent advances in radiologic diagnosis and radiotherapeutics.

EARL E. BARTHE

THAT wound surgery is simply good surgery is brought out significantly in Bailey's introduction to *Surgery of Modern Warfare*,<sup>2</sup> with the observation that if the only message conveyed by the book were to make the distinction clear between wound exci-

sion and débridement, the volume "would be worthy of study by the war surgeons." About this distinction between wound excision and débridement can be written the whole rationale of the local treatment of wounds.

The material contained in the volume at hand is divided into 8 sections and 54 chapters. The first two sections, or a slight one-third of the book, is given over to a consideration of wounds in general, while the remainder of the book is devoted to the consideration of wounds as they affect the various regions of the body. No less than sixty-five surgeons and other specialists have contributed, and from this authoritative and succinct compilation, ably edited by Hamilton Bailey, may be obtained the best picture of war surgery today. Written possibly somewhat hurriedly and under stress of disruptions, this may serve rather as commendation than as adverse criticism since the contributors have daily forced upon them the importance of their observations and the necessity of brevity of expression. Repetitions and inconsistencies in the presentation of material will doubtless be ironed out in subsequent issues and are not to be considered entirely a fault since they represent the diversity of opinions which make surgery a growing science.

Wounds in warfare are considered in relation to the agents causing them, in order that proper appreciation of the possible extent of damage may be obtained. Surgeons with experience in the war of 1914-18 are already familiar with the action of various types of bullet and shell fragment injuries and the extensive disruptive and concussion effects of modern high velocity missiles which may extend far beyond the area of apparent damage. The effect of the aerial bomb, however, has not been so well known and experiences with these wounds are particularly illuminating.

A brief discussion of current concepts of the causes and management of shock is followed by a lengthier discussion of transfusion and infusion, with extensive directions on methods. In view of the rather remarkable advances that have been made in the past year in the use of serum and plasma, it comes as a surprise to see so little space given over to a discussion of it. Some specific instructions regarding amounts of fluids, simple methods for determining patients' needs, and for establishing indications for various fluids would add greatly to the value of this chapter.

The great numbers of burns seen in the present conflict, particularly those involving the face and hands, have made this a most important topic. In view of the recent controversy regarding the use of tannic acid on hands and face, it has been somewhat surprising to see that this question is not more thoroughly discussed.

The chapter dealing with the local treatment of recent wounds emphasizes the principles of treatment and the importance of cleansing to convert a contaminated and devitalized wound into a relatively clean and viable one. The excised wound

<sup>1</sup>THE 1940 YEAR BOOK OF RADIOLOGY. DIAGNOSIS. Edited by Charles A. Waters, M.D. and Whitmer B. Furr, M.D. THERAPEUTICS. Edited by Ira I. Kaplan, B.Sc., M.D. Chicago: The Year Book Publishers, Inc., 1940.

<sup>2</sup>SURGERY OF MODERN WARFARE. By sixty-five contributors, edited by Hamilton Bailey, F.R.C.S., in two volumes. Vol. I. Baltimore: Williams & Wilkins Company, 1941.

must be given "tissue support to prevent or control edema, and immobilization to give complete rest to the injured part." Primary closure, while often possible, should be done only when the patient can be carefully watched. More often the wound should be packed with vaseline gauze and the dressings changed very infrequently. Immobilization on splints does not seem as perfect as that in a plaster encasement, although this method "must be considered to be still on trial." Carrel-Dakin treatment is still applicable in certain types of wounds.

In the local management of infected war wounds, excision is no longer possible and active intervention is undertaken for certain definite reasons only; namely, the presence of retained purulent secretion under pressure, impending or developed gas gangrene, penetrating wounds containing debris and foreign material, and compound fractures in which the bone fragments have led to widespread disruption of tissues. The operations must be carried on with the utmost gentleness, free wide exposure obtained; accurate hemostasis secured; blood clots, foreign bodies and obviously devitalized tissue, especially muscle, excised; and free drainage secured. Here too the closed method of treatment offers the advantages of complete rest and the avoidance of interference with the wound.

Gas gangrene, uncommon during the Spanish Revolution, was frequent in France in 1914-18, and in the casualties in France in the present war. The prophylactic treatment by adequate initial surgical care is stressed and local implantation of sulfanilamide or sulfapyridine is advised. Serum is advisable, though its value is still not established. X-ray treatment is recommended.

The short chapter by Flemming on the bacteriological examination of wounds is one of the most important in the book. Especially significant is his distinction between primary and secondary infection. He brings out not only the potential sources of each type, but the wound conditions which favor growth.

Delayed primary suture of wounds is indicated in those cases in which, after cleansing and excision, some doubt still exists as to the cleanliness of the wound. Secondary suture may occasionally be accomplished after a wound has become clean, preferably between the fourteenth and twenty-first day, before fibrosis becomes too great.

The chapter by McIndoe on skin grafting emphasizes quite rightly that large surfaces should not be allowed to heal by scar tissue, but should be grafted at the earliest possible moment. In the preparation of raw surfaces, the author might stress somewhat more forcefully the use of pressure dressings, and more space could have been devoted to the technique of dressing grafts, the length of time pressure should be maintained, and other details of after care.

The chapter dealing with wounds of the thorax is clearly written, terse, practical, and well illustrated. It is pointed out that in bomb blast injuries the lung is compressed by the chest wall—not exploded by

inrushing air. Many lives may be saved by immediate temporary closure of sucking wounds of the chest. Hemothorax and hemopneumothorax are best treated by aspiration and air replacement in cases which cannot be submitted to early operation. In this way may be overcome the objections to aspiration on the grounds that further lung hemorrhage is encouraged when tamponade of hemothorax is removed.

The acrimonious debate relative to the necessity of operating upon abdominal wounds with visceral damage was settled definitely in the early stages of the war of 1914-18. At the present time cases are classified into those in which patients are in good condition and operable, in collapse but capable of resuscitation, and in a dying condition and beyond aid. Time should be spent in preparing patients for operation, with fluids, warmth, and sedatives, regardless of the general condition. If active hemorrhage is present, resuscitory measures are started and operation is begun as soon as preparations are completed. The keynote of success is gentleness and timeliness of operation rather than speed. Wounds of exit and entrance are excised as in other wounds, but this is deferred until the laparotomy has been completed. A midline incision is the best all-around exposure, although the transverse incision deserves wide usage. The methods of dealing with various types of intra-abdominal lesions are given in separate chapters.

The chapter concerning the use of tourniquets is especially enlightening and the instructions and caution in their use are valuable. Interest in the immediate care of blood vessel injuries must of necessity center largely upon rapid and safe exposure for the purpose of controlling hemorrhage. Injured vessels must be exposed for a good distance above and below the site of injury, and accompanying structures, especially nerves, must be identified. Repair of blood vessel injuries is described briefly and reference is made to the use of heparin in the conservative management of vascular wounds.

Secondary hemorrhage, during 1914-18, was noted as diminishing in frequency with improvement in wound excision. Thus the prophylaxis of the condition is clearly indicated. Immediate control is best obtained by pressure rather than by tourniquet, which may further devitalize already badly devitalized tissues. In the operative control of the hemorrhage, ligation of the actually bleeding vessel is the method of choice. Proximal ligation of the vessel, except in case of gluteal hemorrhage, is not advised. Reference is made in several places to the dangers of the application of heat to badly vascularized extremities. Two chapters are devoted to the management of arterial hematomas, traumatic aneurysm, and arteriovenous aneurysm.

The chapter dealing with methods of applying traction to limbs, while adding nothing new, presents this subject in a clear, practical manner. The Thomas splint is carefully described as are also the Thomas frame, the Braun splint with its various

modifications by Boehler, and the many uses of Cramer wire.

One of the largest chapters in the book is devoted to the use of plaster-of-Paris. Careful detailed instructions are given concerning the application of plaster to all parts of the body, and a host of practical suggestions are made.

Wounds of the hand are treated on the same principles as wounds elsewhere. Primary nerve repair, where possible, is advised, but tendon suture is seldom permissible. Splinting in the position of function as advised by Kanavel is justly advocated as an essential primary principle. Many refinements of technique and methods of soft tissue repair are not mentioned, probably because in the author's opinion such care is not usually possible in wartime injuries. However, certainly in civilian air-raid casualties the opportunity must often present itself to do a really "bang up" job on a severely injured hand with primary nerve and tendon repair and primary skin grafting.

The chapter on infected wounds of the hand conforms in general to the classical teachings of Kana-

vel. It is difficult for the reviewer to accept the pronouncement that the warm moist pack is being supplanted by dry heat, and still more difficult to be impressed by the rotation dressings of eusol, hydrogen peroxide, magnesium sulphate, and normal saline applied every 4 hours in rotation. Iselin's incisions for tenosynovitis with through and through drainage of the web spaces are also difficult to accept.

Wounds and infections of the foot are considered both from the standpoint of wound care in general and from the standpoint of functional requirements of the foot itself.

Two final chapters deal with knee joint and hip joint injuries.

A reading of this excellently prepared volume strengthens one in the conviction that the war surgeon must be capable of dealing intelligently with emergency surgery anywhere on the body. The medical units upon whom will fall initially the great mass of wounded must be made up of well trained, quick acting surgeons who are firmly grounded in surgical principles. It is to men of this type that the volume will be most helpful. MICHAEL L. MASON

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

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Fig 1 Photograph of the liver in a case of uncontrolled diabetes mellitus, taken with an endo-copic camera.  
The tip of each lobe is high lighted

*Intra-Abdominal Photography in Color —  
Thomas N. Horan and C. Graham Eddy*

# SURGERY

## GYNECOLOGY AND OBSTETRICS

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### INTRA-ABDOMINAL PHOTOGRAPHY IN COLOR

THOMAS N. HORAN, M.D., and C. GRAHAM EDDY, Detroit, Michigan

TO include in a hospital chart a photograph in color of an altered structure together with a report on the micro-pathology of the same tissue will add value to the record. This is particularly true of intra-abdominal disease, in the presence of which the usual methods of physical diagnosis, as palpation and auscultation, are often unsatisfactory and the laboratory tests inconclusive.

The photograph of the liver (Fig. 1, frontispiece) shown in this article was taken by a camera attached to the eyepiece of a peritoneoscope. Biopsy photomicrographs from the same case are reproduced in Figures 2 to 4.

The case history need only be briefly outlined since the intent of this paper is to describe a technique for intra-abdominal photography. The patient is a white male, aged 43 years, with an uncontrolled diabetes mellitus, the fasting blood sugar being 337 milligrams per 100 cubic centimeters. He is one of several cases in a study of liver changes in the diabetic. The peritoneoscopic examination was reported as follows: "The liver is normal in color, the edges are soft, round, and flexible. There is a filigree scarring over the surface of the dome on the right side, which is otherwise quite normal. Three biopsies were taken for hematoxylin and eosin, fat, and glycogen stains." The photograph shows the

region of the notch of the liver with portions of the right and left lobes, and the round ligament as it approaches the porta. The tip of each lobe is high-lighted.

Not observed by the examining eye but suggested in the photograph is a greasy appearance of the surface of the liver which may be explained by the increased fat content shown in the biopsy stains. There is an interesting reflection of the round ligament on this surface which appears as an elbow of light extending over the upper portion of the left lobe. There are reasons to hope that the careful, leisurely scrutiny of similar enlarged photographs or their projection on a screen may reveal details of value in diagnosis which are not appreciated during the time of routine peritoneoscopy.

Photographs in other cases have given some additional information. In a case of syphilitic hepatitis with a liver partitioned by broad bands of scar, it was possible in the photograph to discriminate between the lobes involved in the syphilitic process and other lobes which represented only a vigorous regenerative effort. The syphilitic liver tissue was darker in color and covered with a delicate netting of scar; the new liver tissue was light brown in color and smooth, the biopsy showing regenerating liver cells. In cases of cirrhosis the roughened surface of the liver is emphasized by points of light which mark

From Eloise Hospital, Eloise; and Harper Hospital, Detroit.



each separate nodule. A final evaluation of the merit of intra-abdominal color photography as a contribution to diagnosis cannot be made until more photographs are taken.

In the paragraphs to follow the separate pieces of apparatus are reviewed and the procedures employed in obtaining the illustration are recounted. Mention is made of a few of the obstacles encountered

*The camera* Two makes of endoscopic cameras have been manufactured for use with the peritoneoscope: the Gullbring-Jacobaeus endoscopic camera made by the Kifa Instrument Company in Stockholm, Sweden, and more recently an American-made camera of similar design. Pictures from both cameras are sharp in focus and the images are clear. A field-finder incorporated in each camera holds the view except during the moments of exposure when a prism is moved aside and all light strikes the film.

*The camera standard.* Since the exposure time is one-half second it is essential to steady the camera, which must be held in any plane over the operating table. The base of the standard is weighted and to the upright is attached a cantilever arm using a watch-type, flat steel spring to balance the weight of the camera. Near the free end of the arm is a universal joint. From this extends a threaded screw connection to the camera tripod socket.

*The light* When light is passed through a complex optical system, a percentage\* is absorbed by each lens in the series. For this reason the "grain of wheat" lamp on the peritoneoscope is an inadequate source of light for photography in color. In Figure 5,A is shown the type of lamp now being used. It is a tubular bulb, one-quarter inch in diameter (T-2) and burns normally at 24 volts and one half ampere. It is covered with a clear plastic coating to prevent shattering. For our photograph two of these lamps are placed in tandem on a "light-carrier" (Fig. 5). These lamps together may be overvolted to 40 volts and 1.5 amperes. Since this is just below the melting point of the filament, the lamps are burning at their top light efficiency. Their life at this top burning is 10 to 20 seconds. The curved reflector (Fig. 5,B) of the light carrier is

chrome-plated, highly polished, and increases the light 50 per cent. In this manner the equivalent of the light from an 80 watt lamp may be directed onto a field 2 inches in diameter and at a distance of 1.5 to 2 inches. (To compare the light intensity with that of a lamp commonly used in the home is quite inaccurate, but is an expression that can be understood.)

*The lamp base.* Along the thickened rim of each lamp base (Fig. 5,C) are bored five wells 1 millimeter in diameter and 1 millimeter deep (Fig. 5,D). Into these a steel pin (Fig. 5,E) is placed and used as a key to turn the lamp into its receptacle.

*The power source of the light* The power source of the light is two 45 volt dry batteries in parallel. This is well under the limit of complete safety which is considered to be 60 volts. The current is regulated by a rheostat and measured by a voltmeter and ammeter.

*The film* The color film used is the fastest to be obtained; and possesses dramatic color values. The transparency obtained with the endoscopic camera is 4.5 millimeters in diameter, from which high quality wash off relief prints 3 inches in diameter have been made (Fig. 1). The size of the projected image is adequate for lecture room demonstration.

#### TECHNIQUE

The procedures employed in taking the photograph begin with the guiding of the light-carrier and its rod extension (Fig. 5,F) along the side of the peritoneoscope trocar, which is already in place. By the use of a hemostat with long narrow pointed blades the opening into the peritoneal cavity is sufficiently enlarged to admit the light-carrier which may be shoehorned between the blades into the pneumoperitoneum space. A single deep silkworm suture is taken between the rod and trocar in order to prevent the escape of air between these instruments. In this way the domed air space overlying the viscera is preserved, the pneumoperitoneum pressure being 12 to 18 millimeters mercury. Proper lighting of the field is checked with the lamps burning at low intensity. When the picture is taken the lamps are overvolted and the camera shutter is opened. The patient is

\*The average is about 5% for each glass air surface



Fig. 2. Biopsy section (hematoxylin and eosin,  $\times 87.5$ ). There is some increase in fibrous tissue about the trinity and round cell infiltration. The liver cells contain a number of small and medium sized vacuoles.

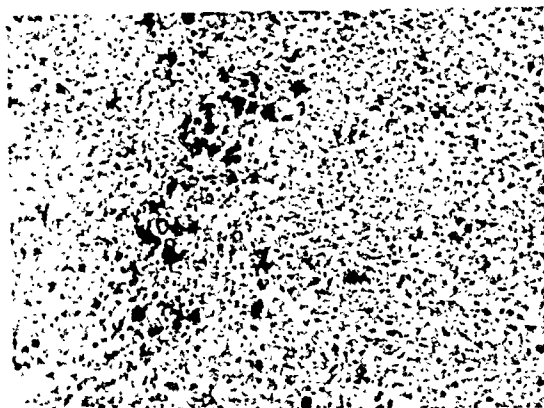


Fig. 3. Biopsy section (Sudan IV,  $\times 87.5$ ). This section shows that the vacuoles take the fat stain.

asked to hold his breath during the time of exposure. The time required for the examination including a diagnostic survey, the biopsies, and photograph need not be more than 30 minutes.

**Obstacles.** Many obstacles not anticipated in planning for the technical procedure of intra-abdominal photography were encountered. A few are of sufficient interest to be described, and of these the need for ever-increasing light intensities presented the chief difficulty. As stated previously, the small lamp supplied with the peritoneoscope was an insufficient source of light, and when over-volted required exposure times of 15 to 30 seconds; with slower films a full minute.

Efforts to obtain very short exposures by the instantaneous flashing of lamps of various types failed to produce more than the faintest outlines on color film. Nor did the flashing of lamps at higher voltages—to more completely consume the lamp filament—impressively increase the light values. It has not yet been possible to make a photoflash lamp using a quarter inch or T-2 type of bulb.

During these experiments with lamps, the glass occasionally would crack and the need for a protective coating became apparent. A clear plastic outer coating was applied and has been satisfactory. Sterilization in the autoclave would cause fogging and peeling of the plastic unless the lamps were placed in a

corked test tube from which all moisture had been driven by heating.

Another problem involved the escape of pneumoperitoneum air between the trocar and the rod of the light-carrier. Various trials with rubber dams and sliding corks were unsuccessful. It was learned that a suture taken deep into the subcutaneous fat between the instruments would in most cases hold the pneumoperitoneum.

In the earlier experiments the peritoneoscope was introduced through the cannula of one trocar, and the light through an entirely separate cannula often placed at a point several inches away. Because of this arrangement it was possible to observe with the peritoneoscope the passage of this second trocar through

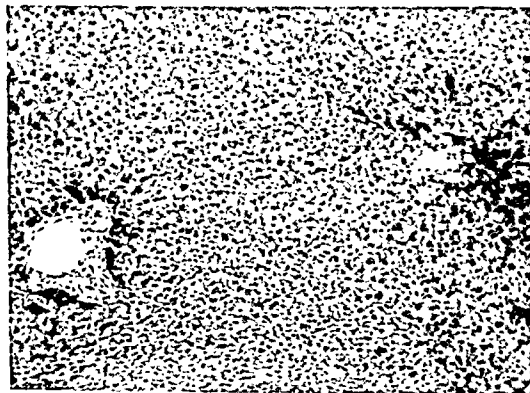


Fig. 4. Biopsy section (glycogen stain,  $\times 87.5$ ). There is an impoverishment in the glycogen content of the liver.

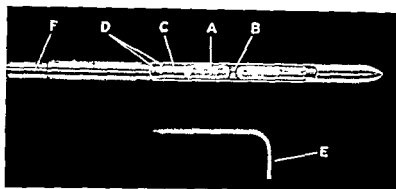


Fig. 5 The "light-carrier" A, lamp, (T-2 bulb, G F), B, reflector, C, lamp base, D, well, E, key, F, rod extension

the anterior abdominal wall. Sometimes the peritoneum could be seen to tent far into the air space before the point of the instrument would pierce the lining membrane. A curious misadventure occurred in a single instance when a trocar, placed at its usual depth, could not be maneuvered freely in the intra-abdominal space. Observation with the peritoneoscope revealed that it had passed *exactly* between the layers of the falciform ligament without entering the peritoneal cavity. The point of the stylet was impinging on the round ligament.

The presence of motion within the abdomen has presented, fortunately, only a minor difficulty. Since local anesthesia is used the wide excursions of the diaphragm may be halted when the patient holds his breath. Peristaltic activity is gentle and intermittent. Expansile pulsation in the section of the liver being photographed moves along the axis of

the object lens of the peritoneoscope and produces little apparent motion. The thrust of the abdominal aorta is transmitted to all structures in the upper abdomen. From pictures taken to date it seems probable that soft livers (hepatitis) will better absorb this motion and give sharper images than hard, fibrous livers (cirrhosis).

A technique which requires the handling of two movable parts within the free pneumoperitoneum space requires an assistant and remains a somewhat difficult procedure. A trocar is now being made with two air locks through which the light-carrier and then the peritoneoscope may be introduced. This trocar will have an outer diameter of 12 to 13 millimeters and is designed to support the lamps in a proper relation to the object lens of the peritoneoscope. The use of a single instrument of this type should greatly simplify intra-abdominal photography.

# COMPRESSION OF THE HEART PRODUCED EXPERIMENTALLY

ARNALDO YODICE, M.D., Buenos Aires, Argentina

IT is my purpose to record observations that I have made in a study of compression of the heart produced experimentally. Most of the observations that I shall record are of a confirmatory nature. Some of the observations are original. The total amount of experimental work that has been done on the subject of compression of the heart is not great. Claude S. Beck (2) in 1929 was the first to produce the condition experimentally. He produced it by the injection of Dakin's solution into the pericardial cavity of dogs. At that time the disease was variously referred to as Pick's disease, adhesive pericarditis, mediastinopericarditis, and constrictive pericarditis. Using this experimental method for the production of the disease, Beck and Griswold (7) in 1930 were able to make observations and studies concerning its physiology and operative treatment. They reported a series of 50 experiments in 11 of which the syndrome of cardiac compression was observed in various stages of development. In some of these animals the condition was completely cured by removal of the pericardial scar. They showed that the heart became smaller as the syndrome developed, and also that the minute volume output of the heart was diminished. They also found congestion in the liver and a fibrinous and fibrous exudate on the surface of the liver. These developments could not be explained on an infectious basis. They also showed that the syndrome could be produced without adhesions. At about this time Churchill (9) did the first successful operation in this country. In 1935 Blalock and Burwell (8) made determinations on the pressure in the thoracic duct. They produced the condition in 2 dogs by the injection of aleuronat into the pericardial cavity.

In one of these animals they found that the pressure in the external jugular vein at the end of 3 weeks was 120 millimeters of water, the pressure in the femoral vein was 140 millimeters of water, and the cerebrospinal fluid pressure was 240 millimeters of water. The autopsy examination showed "concretio cordis." The second animal showed signs of illness 17 days after the introduction of aleuronat. The pressure in the external jugular vein was 155 millimeters of water, in the femoral vein 175 millimeters of water, and in the thoracic duct 200 millimeters of water. According to these experiments the pressure in the lymphatic system is increased in this condition.

The most important contribution to this subject was made by Beck when he introduced a new concept to cover this type of disease. His concept was that some diseases of the heart are intrinsic in nature; others are extrinsic. This condition under discussion he claimed was one form of extrinsic disease and he called it compression of the heart. He divided compression into two classes, one acute the other chronic. He introduced a triad of signs for diagnosis. The Beck (3) triad for acute compression was (1) a small quiet heart, (2) a rising venous pressure, and (3) a falling arterial pressure. The Beck triad for chronic compression was (1) a small quiet heart, (2) a high venous pressure in the arm, and (3) ascites and a large liver. Rotation of the heart and angulation of the heart were other forms of extrinsic disease. Adhesions with traction in the long axis of the heart, he showed, were not a form of extrinsic disease. Up to this time writers used the term heart tamponade to designate acute compression. Beck was the first to show that heart tamponade was really compression in the acute form, and he was the first to show its relationship to chronic compression or Pick's disease. It is logical that this terminology should be adopted univer-

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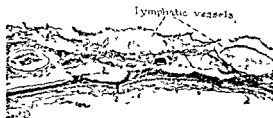


Fig 1 Photomicrograph of gall bladder showing enlarged lymphatic channels

sally, and that the terms adhesive and constrictive pericarditis and heart tamponade should not be used

**Experiments.** For this study I attempted to produce cardiac compression in various ways. The following irritants were used in the pericardial cavity—Dakin's solution, hydrochloric acid in strengths of 1, 5, and 10 per cent solutions, tincture of iodine, collodion, hot, normal sodium chloride solutions, aleuronat, and iodized talc. Rubber bands were placed around the heart and in several experiments the pericardium was reduced in size by plication with silk sutures. The observations carried out in these experiments were as follows: size of the heart by x-ray, venous pressure determinations, electrocardiograms, determination of pressure in the thoracic duct, production of lymph, postmortem studies, results following removal of the compression agent and observations on the coronary arteries.

**Results.** It was difficult to produce chronic compression of the heart because in many experiments death occurred early from acute compression. In other experiments the compression was not sufficient to produce the clinical syndrome and repeated operations were carried out to increase the degree of compression. In all, 146 experiments were done. Twenty-three animals were operated upon twice, 15 were operated upon three times, and 3 were operated upon four times. Acute compression and death occurred in 27 experiments a few hours after operation, and 6 animals were lost within a few days from the operation. This latter group showed signs of both acute and chronic compression. Chronic compression developed in 38 experiments, in 14 it was severe and in 24 not marked.

I found that Dakin's solution was the most efficient method of producing cardiac compression. The initial reaction to the introduction of Dakin's solution into the normal pericardium of dogs consist of tachycardia and hemorrhage. The hemorrhage takes place from the surface of the heart and from the pericardium and is due to the erosive action of the solution. Subsequently the parietal pericardium and epicardium become thickened. Frequently, but not always, the parietal scar becomes adherent to the epicardial scar. Sometimes a layer of fluid is found between heart and parietal scar. The tachycardia can be prevented by the use of procaine applied to the surface of the heart before the Dakin's solution is used (13).

In 16 of the 38 experiments in which clinical evidence of compression developed, I observed the degree of compression to improve after it developed. This improvement was due to absorption of fluid in the pericardial cavity or resolution of thick edematous scar. It is doubtful whether a dense fibrous scar around the heart can stretch or relax sufficiently to reduce the degree of compression after it has once formed. In human patients a dense scar has a tendency to remain stationary or to undergo further contracture with an increase in the compression. If the scar is made up of young connective tissue cells, fibrin, and edema, it is possible for the compression to undergo a reduction in degree with improvement in the clinical condition.

Venous pressures were measured by the direct method from the jugular vein. A right angled glass tube filled with physiological solution of sodium chloride was attached to the vein by means of a needle and the solution was allowed to run into the vein. The height in centimeters was the pressure in the vein. It was my experience that when the venous pressure rose to 8 centimeters within the first 24 hours the dog would die from acute compression. This is not in accord with the experience of Elkin in his patients with stab wounds of the heart. He found pressures of 30 to 40 centimeters of sodium chloride in traumatic cases. Beck (6) placed the fatal level for the acute condition in dogs at 15 to 20 centimeters. I observed in my experiments that the venous

pressure during the next few days either went up or it went down. If the venous pressure showed an early rise and later fell off to nearly normal levels, the animal did not develop ascites. I confirmed Beck's observation that ascites, which occurs only in the chronic condition, appears when the venous pressure rises to about 15 centimeters. It might be stated that it is ascites, and ascites only, that brings the patient with chronic compression to the physician. After the chronic condition becomes established, I obtained venous pressure determinations as high as 30 centimeters of normal sodium chloride solution. In Beck's (5) series of patients the lowest venous pressure was 18 centimeters and the highest was 42 centimeters. It is interesting that the threshold for ascites expressed in terms of venous pressure is the same in the experimental condition as it is in the human patient.

I was interested in making a study of the relationship between ascites and venous pressure. Several experiments were carried out in which warm physiological solution of sodium chloride was injected into the abdominal cavity. I found in these experiments that the pressure in the femoral vein and in the jugular vein became elevated when fluid was introduced into the abdomen. The introduction of 6 liters of fluid into the abdomen elevated femoral vein pressure to 25 centimeters and jugular vein pressure to 10 centimeters. Conversely, in our experiments in which ascites formed as a result of the compression of the heart, it was found that the removal of ascitic fluid produced a fall in the venous pressure. In one experiment removal of 6 liters of ascitic fluid resulted in death of the dog. This is in agreement with Beck's (4) teaching that the high venous pressure is a protection when the heart is compressed and this should be held in mind when the abdomen is tapped. A tight binder should be used after tapping to keep the venous pressure elevated.

An increase in the resistance in the pulmonary vascular bed also increased venous pressure. The injection of one liter of fluid into the pleural cavity increased the jugular vein pressure to 5 centimeters and the injection of 2 liters killed the animal. Increased pressure in the alveolar bed also increased venous pres-

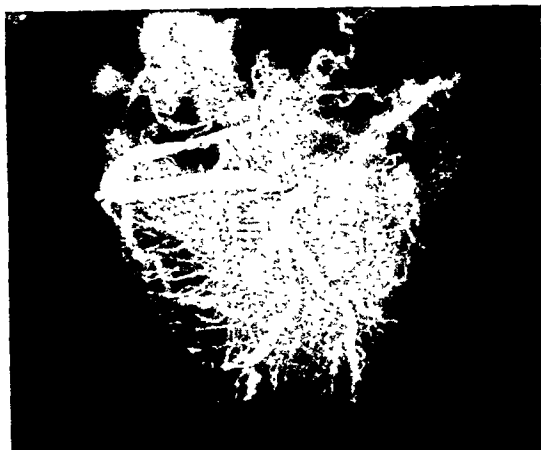


Fig. 2. Heart from dog after production of chronic cardiac compression. The coronary arteries were injected with barium-gelatin mixture and roentgenogram of the specimen was taken. The coronary arteries in this and in other compressed hearts are larger than normal.

sure. This was demonstrated by introducing air into the trachea by means of an intratracheal catheter. Marked rises in venous pressure were produced by forcible distention of the lungs. It was found that forceful intermittent insufflation raised jugular pressure to 8 centimeters. It was also found that continuous pressure in the pulmonary bed raised jugular pressure to 15 centimeters and a fall in arterial pressure also occurred. These facts have clinical application because if the lungs are forcibly blown up during operation on the heart, the right ventricle can be thrown into failure because of the increased resistance in the pulmonary vascular bed. I understand that this occurred in one of the clinics in this country but no explanation was given for the death. The heart failed when the lungs were forcibly blown up during operation.

*Roentgenographic studies.* The size of the cardiopericardial shadow was increased during the first few days after the injection of Dakin's solution. The increase in size was due to fluid and edema around the heart. The shadow became smaller after the fluid was absorbed. After the cicatrix became organized and underwent contracture, the shadow actually became smaller than it was under normal conditions.

*Lymphatic studies.* These studies were carried out according to the method by Jappelli

used by Lee and Beck (1). A segment of vein is isolated where the thoracic duct joins the venous cistern at the junction of jugular and subclavian channels. A glass tube is introduced into this isolated segment to measure thoracic duct pressures. Lymph flow was determined by direct measurement. In one experiment in which the venous pressure measured 19 centimeters, I found the pressure in the thoracic duct to rise in the manometer to 27 centimeters. In another experiment, the venous pressure was 20 centimeters, and the thoracic duct pressure rose to 26 centimeters in the manometer. Pressure applied to the abdomen forced lymph out of the abdomen and the level rose to 80 centimeters. In 2 other experiments in which chronic compression had developed, the lymph flow was measured. In these experiments I did not find any definite lymphagogue effect.

*Electrocardiographic studies.* Low voltage and slurring were found in the electrocardiograms.

*Autopsy examinations.* The animals with chronic cardiac compression were waterlogged. All veins were distended, many were dilated. The lymphatics in the neck were engorged with lymph. Engorged lymphatic channels were found in the gall bladder (Fig. 1) and in the mesentery of the intestines. The liver was engorged with blood and enlarged. Fibrin was deposited on the capsule of the liver. The interstitial fibrous tissue is increased in the liver. The pericardial scar was variable in thickness and organization. In some cases the scar tissue extended over the venae cavae. The heart showed some degree of atrophy. The presence of adhesions was variable. The coronary arteries were studied after injection with barium. It was my impression that the large coronary arteries were larger than normal. This might be related to increased resistance in the peripheral arterial bed. That the peripheral pressure in the myocardial vascular bed is increased is an assumption. It has

not been demonstrated. The observation of large coronary arteries was made in many specimens and is illustrated in Figure 2. It is possible that the atrophy of the musculature makes the arteries relatively large. The brain showed definite signs of edema.

#### CONCLUSIONS

Chronic compression of the heart was produced experimentally by the introduction of Dakin's solution into the pericardial cavity, by the introduction of iodized talc into the pericardial cavity, and by placing rubber bands around the heart. The pressure in the lymphatic system is increased when the heart is compressed. The flow of lymph from the thoracic duct was not increased. The electrocardiograms showed low voltage in all leads. The interstitial tissue in the liver is increased. The chronic condition is cured by resection of the compression scar. The coronary arteries appear to be larger than normal in chronic cardiac compression (Fig. 2).

The removal of fluid from the abdomen reduces venous pressure. Forcible distention of the lungs during resection of compression scars increases resistance to the flow of blood through the lungs and elevates venous pressure. Both of these points have clinical application.

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# INFUSIONS OF BLOOD AND OTHER FLUIDS INTO THE GENERAL CIRCULATION VIA THE BONE MARROW

## Technique and Results

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IN 1936, while conducting experiments on transplantation of marrow between animals, it was observed that if two needles were inserted into the marrow cavity of the femur of a rabbit, one at either end of the bone, and 5 cubic centimeters of salt solution injected through the proximal end of the bone, only about 2 cubic centimeters would come up through the distal needle. Repetition of the injection yielded the same results. Examination of the muscle and other tissue adjoining the area of the injection revealed no infiltration with the injected fluid even when the latter was colored. It was evident, therefore, that some of the fluid was being absorbed into the general circulation as fast as it was being injected. Subsequent experiments demonstrated this fact in a more convincing manner (9).

When mercury is injected into the marrow cavity of the sternum (9) or is injected into the tibia and humerus of infants (Fig. 1), the metal may be seen by fluoroscopy to escape rapidly through the emissary veins into the general venous circulation. It has been demonstrated that micro-organisms injected into the bone marrow of guinea pigs may be found in various organs almost immediately after injection (1). These facts indicated the existence of anatomical relationships between the vessels of the bone marrow and the general circulation of a nature heretofore unsuspected. Advantage has been taken of this knowledge to use the marrow cavity as a path for the purpose of the rapid introduction of blood as well as other fluids into the blood stream (10).

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## METHODS

The technique differs slightly depending on the bone that is selected. In the sternum of adults the site of election for the puncture is either the manubrium (Fig. 3), or the body of the sternum midway between the angle of Louis and the xiphoid process. After preliminary injection of the skin, subcutaneous tissue, and underlying periosteum, with procaine, the needle is inserted vertically, with the bevel up and the periosteum is penetrated with a to and fro twisting motion until a good foothold is obtained (Fig. 2, a). Then the needle is tilted until it makes an acute angle of about 30 degrees with the surface of the skin and, with a semicircular to and fro motion, the anterior plate of the sternum is penetrated (Fig. 2, b). A definite sensation of diminution in the resistance of the bone, amounting sometimes to a "trap-door" effect, is felt when the cavity is penetrated. Practice on the cadaver enables one to acquire a clear appreciation of this diminution in resistance.

Once the marrow cavity is penetrated the ball guard is adjusted and the stylet is removed from the inner needle (Fig. 2, c). A syringe containing about 1 cubic centimeter of salt solution is attached to the needle and gentle aspiration is applied. If the needle is properly placed and the marrow is vascular the blood-marrow mixture will, upon aspiration, flow into the syringe with very little effort (Fig. 2, d). The degree of force required to aspirate the marrow gives some indication of its density. Only 0.1 cubic centimeter or less of marrow should be aspirated. The inner needle with the syringe is then removed, flushed through with clear salt solution (Fig. 2, d, inset) and reinserted in the outer needle while alternately aspirating and injecting salt solution through it. The pur-





Fig 1 Roentgenograph of the body of a newborn in which Mercury was injected at the upper end of the tibiae (arrows) and in the humeri

pose of this step is to remove air from the lumen of the outer needle. At this point about 1 to 2 cubic centimeters of salt solution is injected into the marrow slowly (Fig. 2, e) Immediately afterward the inner needle is removed (Fig. 2, e, inset) and the adapter from the air-free, salt solution filled rubber tubing and reservoir is attached to the salt solution filled outer needle (Fig. 2, f) Swiftmess of manipulation is important to insure against clotting of any marrow in the needle

Penetration of the bone is accompanied by moderate discomfort. Aspiration of the marrow gives the patient a sensation of drawing which is slightly unpleasant, when the salt solution is being injected there is also slight discomfort. Once these steps have been completed no further discomfort is experienced during the infusion. A few of the children went to sleep while the infusion progressed.

In most instances the flow from the body of the sternum is slow (2 to 4 c cm. per minute) at first, then within 10 to 15 minutes it is accelerated. If it is necessary to add any material to the burette, it is essential to take the precaution of clamping the tube below the dropper before bringing the burette down. This is to prevent lowering the pressure in the tubing, which would allow the marrow to run up into the needle and plug its lumen. In a child under 3 years of age, the marrow in the sternum is probably not developed to the point that it will allow this site to be used. The sites of choice in babies or young children are the upper portion of the tibia or the lower portion of the femur, at the metaphysis. We have not had enough experience with this method in infants under one month of age to judge of its value in this age group. In a baby, 8 days old, the infusion was abandoned because of a slow rate of flow. But in another, 7 weeks old, 145 cubic centimeters of blood were infused without any difficulty. To avoid the possibility of injuring the epiphyseal cartilage, it is desirable that the needle should be pointed toward the diaphysis of the bone (Fig. 3). The needle should be inserted about 2 to 3 centimeters below the proximal end of the tibia, or in the femur, about the same distance above the external condyle; once the flow has started, the leg should be raised slightly above the level of the body. In children above 3 years of age, and in some adults, it is preferable that the puncture be made in the manubrium of the sternum. The marrow cavity of the manubrium is relatively larger than that of other bones in young children and in most adults the rate of flow is more rapid in the manubrium than in the body of the sternum. Great caution and very little force are necessary in penetrating the anterior plate of the manubrium in children. Needles 15 to 25 centimeters long only, should be used, to guard against penetration of the posterior plate. The thinness and softness of the bony plates of the sternum in children do not allow as easy a differentiation to be made between the bone and the marrow as in adults. It is only by aspirating with the syringe and obtaining marrow that the operator can be assured that the needle is in the proper loca-

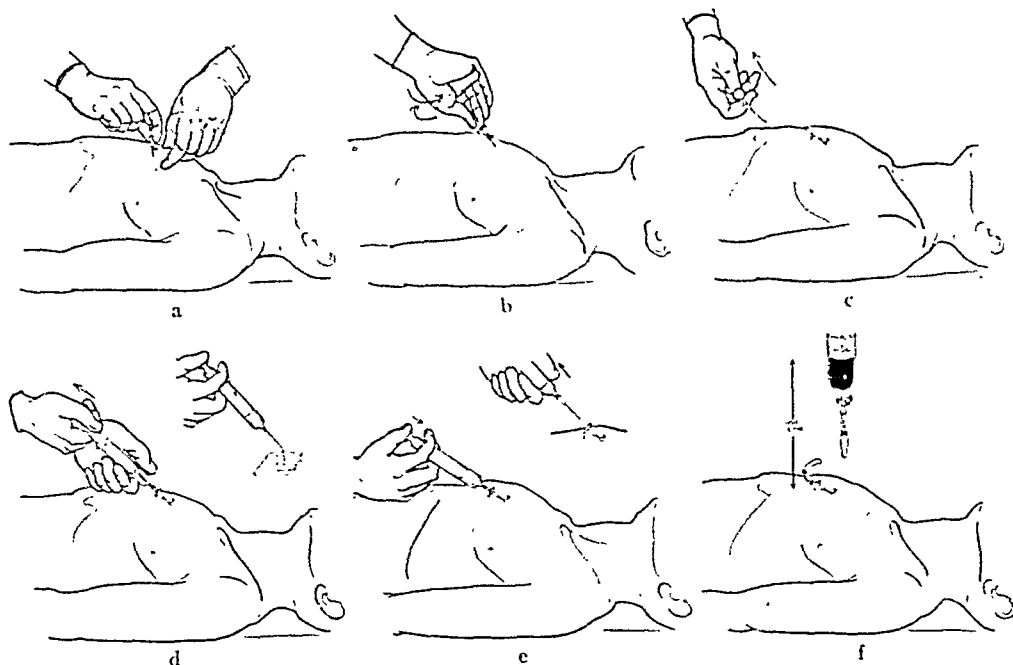


Fig. 2. Steps of the technique for infusing substances into the bone marrow of the human sternum. a, Penetration of skin, subcutaneous tissue, and periosteum; b, entering the bone and marrow, semirotatory motion; c,

removal of stylet, adjustment of guard; d, aspiration of marrow, inset, flushing out internal needle; e, reintroduction of needle, injection of saline. c. inset, removal of internal needle; f, connection to gravity infusion apparatus.

tion.<sup>1</sup> In Figure 3 is illustrated the type of a needle used for these infusions. Needles of similar design can be applied to the same end. The purpose of the double needle is to keep from contaminating repeatedly the external needle with pieces of bone marrow when several aspirations had to be tried during the same puncture. Such repeated aspirations increase the likelihood of producing clotting inside the needle with consequent obstruction.

Several precautions should be kept in mind. In general, no material should be injected unless a blood-marrow mixture has been clearly obtained by aspiration. If no blood-marrow mixture is obtained upon aspiration it is because: (a) The needle may not be in the marrow cavity. The point of the needle may be in the substance of the bone or beyond the posterior bony limits of the cavity (posterior plate of the sternum or posterior surface of the

tibia or femur) or to one side of the cavity. (b) The marrow is not sufficiently vascular because of replacement by cellular infiltration, fibrous tissue, or bone proliferation. The low incidence of failures in the series now being reported indicates that such changes are not common. (c) The distal opening of the needle may be lying against a spicule of bone. Turning the needle about a semicircle may clear the obstruction.

When the sternum is used care should be taken not to penetrate the posterior plate; if the needle projects far out above the skin it is desirable to equip it with a guard adjustable at any desired level. It is essential that a clear impression of the width of the bone and its approximate center be obtained by grasping the sides of the bone between the thumb and forefinger (Fig. 2, a). The needle is then inserted in the center of an imaginary line between the two fingers, to avoid pointing it away to one side of the marrow cavity. No solution should be injected until the air from the lumen of the needle is removed as previ-

<sup>1</sup>The technical details regarding the application of this method in infants and children will be taken up elsewhere (*J. Am. M. Ass.*, in press). In infants, under 6 months of age, it has been found convenient and even desirable to discard the outer, gauge 15, needle and use the inner, gauge 18, needle and stylet only. In view of the narrowness of the marrow cavity in these subjects, the use of the smaller needle will facilitate penetration of the bone and reduce the amount of trauma.

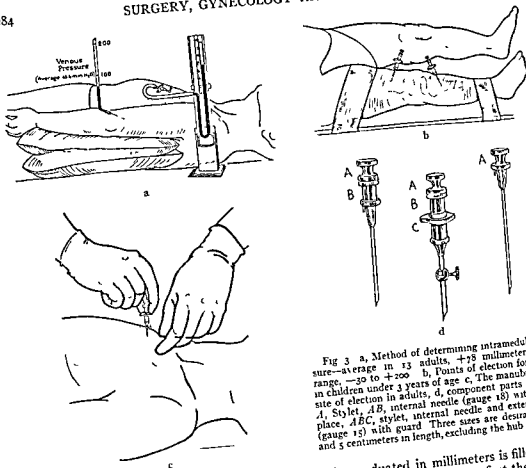


Fig 3 a, Method of determining intramedullary pressure—average in 13 adults, +78 millimeters water—range, —30 to +200 b, Points of election for puncture in children under 3 years of age c, The manubrium is the site of election in adults, d, component parts of needle<sup>1</sup>. A, Stylet, AB, internal needle and external needle in place, ABC, stylet, internal needle and external needle (gauge 15) with guard Three sizes are desirable 2, 3, 5, and 5 centimeters in length, excluding the hub

ously mentioned This precaution is especially important in infants, who, because of their small size, may not tolerate well an injection of even small amounts of air More than the usual care should be exercised to keep the lumen of the needle clear by not allowing a reversal in the direction of the flow in the needle A decrease in pressure in the tubing allows the highly coagulable marrow to ascend the lumen of the needle and to clot, thereby obstructing any further flow If upon entering the cavity no marrow can be removed by gentle aspiration, it is likely that no fluid can be injected Under these circumstances a search for other bones (e.g. tibia) may yield a favorable site Sometimes marrow may be obtained easily from the manubrium when an attempt at the body of the sternum has failed In Figure 3 is illustrated the method of determining the intramedullary pressure A

tube graduated in millimeters is filled with 3 per cent citrate solution, at first the liquid in the tube drops rapidly until it reaches a height of approximately 100 millimeters from the surface of the chest When the level of the liquid has remained stationary for at least 3 minutes but may be displaced slightly by the patient taking a deep breath, a reading is made.

#### RESULTS

To date 52 trials have been carried out in 40 patients, 17 females, 23 males, 33 of these patients were adults ranging in age from 14 to 80 years In one patient it was not possible to remove any marrow or inject any salt solution at three levels of the sternum This patient died after operation about 2 weeks after the attempted infusion, at autopsy it was found that the marrow cavity of the sternum

<sup>1</sup>Needle made by the George Filling & Son Co., Philadelphia.

was small, dense, and with little marrow in it, the bone itself being unusually hard. In 7 instances the infusions were given to children under 2 years—8 days, 7 weeks, 2½ months, 5 months, 6 months, 10 months, 19 months—the needle being inserted in either the upper portion of the tibia or the lower portion of the femur as illustrated in Figure 3.

The needle has been left in place for periods varying from 7 minutes to 30½ hours. The rate of infusion by gravity is governed to a great extent by the density of the marrow. It has varied between 0.4 of a cubic centimeter to 25 cubic centimeters per minute in the manubrium or the body of the sternum of adults; in the tibia or femur of children the average rate of infusion is between 0.5 and 4.2 cubic centimeters per minute with an average of 1.7 cubic centimeters. By means of a syringe, it has been possible to inject as much as 43 cubic centimeters per minute intrasternally. Such rapid rates of injection are justified only when the patient is in shock. Fluids can then be given rapidly into the sternum with the knowledge that the patient does not feel the added discomfort caused by the temporarily increased pressure in the marrow cavity. The amounts infused by gravity have varied between 50 and 2000 cubic centimeters. The manubrium of the sternum was used 20 times, the body of the same bone 20 times, and the clavicle twice. When the clavicle was used the flow was disappointingly slow. This is probably because this bone is unusually thick and its marrow cavity correspondingly small. Though the clavicle is easily accessible the slow infusion rates render it undesirable as a preferred site. In most instances the flow by gravity in the manubrium was more rapid than in the body. The average rate of flow in the manubrium was 3.4 cubic centimeters per minute (range 0.7 to 25.0); and in the body 3.1 cubic centimeters per minute (range 0.4 to 9.1). The same bone has been used as many as three times within 4 days. In one patient, a woman, the manubrium was used on one day and the body of the sternum, on the following

Citrated blood, citrated plasma, 5 per cent glucose solution, and plain physiological salt solution have been infused. In a few in-

stances the infusion was given into the marrow because the usual routes were not available. One of the children (Case 6) was a good example of the type of patient in whom this method would find perhaps its most proper application.

J. H., a boy, aged 6 months, weighed 23 pounds and was edematous and jaundiced on admission to the hospital. His arms and legs were so padded with fat that no veins could be discerned even after long application of a tourniquet. He received three small blood transfusions through the external jugular veins. While the transfusions were being given the boy struggled and the needles came out of the veins. Hematomas and a local cellulitis followed and this made impossible any attempt to re-enter the veins. The red blood cell count at this time was 700,000 per cubic millimeter. The anemia was of the acute hemolytic type (Lederer's). Within a period of 10 days three infusions of citrated blood were given, the first one in the right tibia and the following ones in the right and left femurs, respectively. The red blood cell count rose above 3,000,000 per cubic millimeter and the baby made a slow recovery. A detailed account of this case will be published elsewhere.

Case 24 is another illustration of the use of this method:

E. W., a 25 year old diabetic colored woman<sup>1</sup> developed abdominal pain and rapidly became semistuporous; the blood sugar was 530 milligrams per 100 milliliters of blood and the urine gave a strong reaction for sugar, acetone, and diacetic acid. The patient had had several admissions to the hospital because of coma following alcoholic debauches, gross neglect of her diet, and inadequate insulin therapy at home. In the early morning of the day that we first saw the patient, her coma had deepened, the respirations had become shallow and infrequent, the skin cold, and no pulsations could be felt at the wrist or neck. The resident physician had made several attempts to give insulin and fluids intravenously without success. The veins were collapsed and it was not possible to distend them by the usual means.

On December 30, 1940, at 9:08 a.m., the manubrium of the sternum was punctured; 2 cubic centimeters of a blood-marrow mixture was aspirated. Twenty cubic centimeters of salt solution was injected within 50 seconds. Sugar content of the blood-marrow mixture was: 540 milligrams per 100 milliliters; carbon dioxide combining power was 5 volumes per cent. At 9:10 a.m., 120 units of crystalline zinc insulin was injected into the manubrium. At 9:10½ a.m., 1,000 cubic centimeters of 5 per cent glucose solution was started. The initial rate of

<sup>1</sup>From the Medical Service of Dr. Garfield Duncan, Pennsylvania Hospital.

flow was 11 cubic centimeters per minute, by gravity, from a height of 80 centimeters. At 9 16 a.m., pulse was felt for the first time at the wrist. At 9:21 a.m., pulse was 96 per minute, regular, of fair volume. The patient answered questions. At 9:40 a.m., the pulse was of good volume, the jugular veins distended.

The infusion of 5 per cent glucose was continued at the regulated average rate of flow of 81 cubic centimeters per minute until the patient had been given 1,500 cubic centimeters in about 3 hours. Through a misunderstanding, the patient received the next injection of insulin intramuscularly at 11 00 a.m. She died at 12:15 p.m. At autopsy no fluid or blood was found in the thorax. There was a small orifice admitting a small straight pin on the anterior plate of the manubrium. Otherwise both surfaces of the sternum as well as its interior appeared normal. Before the sternal marrow infusions the patient had had several intramuscular and subcutaneous injections of insulin without any appreciable effect on her condition. Stagnation of the circulation was probably responsible for the poor absorption and ineffectiveness of these injections of insulin.

Case 31 furnishes another illustration of the application of the method in an infant.

B. L. (observed by courtesy of Dr Geist of the Misericordia Hospital) white male, age 7 weeks, had had pyloric obstruction since birth. At the age of 5 weeks a Rammstedt operation was performed, and the usual hypertrophy of the pyloric musculature was found. Following the operation the child continued to vomit and became emaciated—weight approximately 6 pounds. A barium meal revealed almost complete obstruction at the pylorus. It was impossible to detect any veins in any of the extremities suitable for a transfusion. The presence of a gastrointestinal disturbance made it inadvisable to use the intraperitoneal route. The needle was inserted into the lower metaphysis of the left femur and over a 65 minute period, 145 cubic centimeters of blood was infused. The baby was quiet throughout most of the period of the infusion. The following day the plasma proteins were 4.1 grams per 100 milliliter. The baby began to retain all the food and to gain in weight. Seven days following the first transfusion, a second one was given in the right femur. The baby has continued to gain weight and there has been no further vomiting.

There were no immediate or delayed local or constitutional reactions following any of these infusions. For 4 to 5 days following the infusion there was slight tenderness on deep pressure over the site of the puncture. Roentgen ray studies of the bones of the children and of a few of the adults did not disclose any

abnormalities aside from the orifices of the punctures immediately following the infusions or 2 to 3 weeks afterward.

In patients who received infusions of blood there were within 24 hours substantial rises in hemoglobin and number of erythrocytes. There were no statistically significant changes in the total and differential leucocyte counts carried out after 4 of the infusions.

The intramedullary pressure was measured in 9 patients either before or after the period of infusion. In no instance was there a significant difference between these readings. Pressures varied between 40 millimeters and 195 millimeters of water. In most instances the intramedullary pressure corresponded very closely to the venous pressure taken at the same time.

#### ANALYSIS OF STUDY

Substances have been injected into the marrow cavity with the object of influencing the functional activity of its cells (2, 6). The speed with which such materials enter the circulation must make it unlikely that any effect, beneficial or otherwise, is the result of a local action of the injected substances. Such rapidity of absorption also renders open to question the rationale of the procedure of marrow transplantation as recently advocated and carried out in one patient (8). The transplantation was accomplished by aspirating about 5 cubic centimeters of marrow from a healthy donor and injecting it immediately into the sternum of the receiver. Such blood-marrow emulsions probably do not remain *in situ*, but are scattered through the circulation eventually lodging in the capillaries of the lungs.

This type of infusion should find its greatest use when rapid absorption of unchanged substances is the chief object and the intravenous route is not available. Such may be the case in patients with widespread burns, mutilations, generalized edema, circulatory collapse, and in adults or children who have a poorly developed venous system or who have had their veins rendered useless by repeated punctures or by injections of hypertonic solutions. It may find application under circumstances which do not allow the time necessary

<sup>1</sup>From the services of Drs. Thomas and James A. Kelly.

to find a vein and insert a needle in it, and the accessories required to maintain the needle in the vein. In ambulances (automobile or airplane) and in battle field emergency stations, continuous intravenous therapy is often out of the question. The relative immobility of a needle inserted in a bone might then prove a distinct advantage. When dealing with delirious patients or with children whose soft tissues and constant struggling or stirring render it difficult to keep the needles in the veins the procedure may prove advantageous.

Though blood injected into the peritoneal cavity is said to be rapidly absorbed without much change, it appears that in certain disorders chiefly of the gastrointestinal tract, little or no absorption takes place (7).

The method would seem to be contraindicated in generalized infections accompanied by bacteriemia; the long permanence of the needle in the marrow may encourage the localization of a suppurating process at that point. No hypertonic or other irritating solutions should, of course, be infused through this route because of their possible effect on adjacent marrow and bone.

During any infusion into the bone marrow, some fat is conceivably displaced into the blood stream. There seems to be little ground, however, for fearing any such complication as "fat embolism." Harris, Perrett and MacLachlin calculated the minimum lethal dose of human tibial marrow fat to be 0.9 cubic centimeter per kilogram of body weight when injected intravenously into a rabbit. This would correspond to a single lethal dose of 63 cubic centimeters for a man weighing 70 kilograms. The marrow selected for infusion must be highly vascular, and it is precisely this type of marrow that has the lowest fat content.

The bone marrow in children contains relatively little fat (3). Bolle found as little as 2.23 per cent fat in the marrow of a 7 year old child. The average adult human sternum contains 8 grams of marrow, approximately 25 per cent of which (2 gm.) is fat. When fluids are infused into this marrow, they immediately make their way into the blood stream via the veins nearest the point of injection, so that only a small fraction of the fat content of the marrow is disturbed.

#### SUMMARY

Fifty-two infusions of various fluids into the bone marrow of 40 patients (33 adults and 7 infants) have been carried out. There were no local, constitutional, immediate, or delayed reactions accompanying or following any of the infusions. From 50 to 2,000 cubic centimeters of fluid have been infused at a rate of flow by gravity varying between 0.4 and 25 cubic centimeters per minute. Either the manubrium or the body of the sternum is the site of election for this procedure. The intramedullary route is indicated whenever a rapid absorption of unchanged substances is desired and the intravenous route is not available.

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# ACUTE APPENDICITIS IN CHILDREN

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**I**N recent years a number of authors have deplored the increasing mortality in cases of acute appendicitis as observed throughout the country. Old age and extreme youth have been emphasized as periods in which the mortality is particularly high. In view of the advances in medical care and in surgical management, this is the reverse of the expected. The experience of various authors reporting the outcome of appendicitis in children within the past few years is summarized in Table I, showing clearly that with one or two exceptions the average mortality for appendicitis with abscess formation or with complicating peritonitis remains unduly high.

Our purpose in this paper is to present the results obtained in the treatment of acute appendicitis in infants and children at the Babies' Hospital over a period of  $5\frac{1}{2}$  years, and to suggest that with co-ordinated medical and surgical care the mortality rate in the younger age groups can be maintained at a comparatively low level. The records of patients admitted between January 1, 1935 and June 30, 1940, with the diagnosis of acute appendicitis, have been reviewed in detail. This series is in direct sequence with the report of Caldwell covering the period 1930-1935 at the same hospital. Data were tabulated on a "check sheet" similar to that employed by Hudson and Chamberlain.

**Classification.** All cases from which the appendix was removed have been studied personally by the authors. Only cases in which the primary disease was in the appendix are included. When either the pathological report or the operative impression was not one of appendicitis, the case was deleted. In order that no fatality might be omitted through clerical error, all hospital deaths for the given period were checked.

The cases were divided into two groups (1) acute appendicitis without perforation, (2) acute appendicitis with perforation. Group

2 was further subdivided. These subdivisions of "localized," "spreading," "diffuse," and "generalized" peritonitis are admittedly impressions for, as Ladd (15) has said, "No surgeon really knows how diffuse the process is unless he has done a very improper operation." "Generalized peritonitis" was reserved for a relatively small group of patients. Such classification was felt to be justified as they all subsequently developed multiple purulent intra abdominal collections. Special consideration was given to abscess. Instances in which there were a few cubic centimeters of pus adjacent to a perforation have been grouped as "localized peritonitis." "Abscess" implies a large suppurative pocket. Table II gives a perspective of the entire classification.

**Etiology.** In recent years fecal concretions, exanthemas (6), infestation with oxyuris vermicularis (3), and trauma (14) have been considered as contributing factors to the development of appendicitis. Although fecaliths and obstructing bands were occasionally found, without adequate controls we were unable to relate their presence to the causation of this disease. Pinworms were found in only two instances, although all removed appendices were subjected to histological examination. We agree with Botsford that this infestation is not a significant etiological factor. Three patients gave a history of a recent exanthema. Measles and scarlet fever complicated the postoperative course once each. Recent trauma of significant severity was found in 5 instances. Four of these appendices were found to be perforated. We feel that such an event is of more importance in suggesting an erroneous diagnosis of ruptured viscus than in explaining the etiology.

**Sex and race.** One hundred seventy-seven patients were males and 149 females. This is more in accordance with the ratio of Hudson and Chamberlain than with that of authors who stress a high incidence in the male. There were 298 white patients and 28 negroes in the present series.

TAYLOR, HODGES: ACUTE APPENDICITIS IN CHILDREN

TABLE I.—SUMMARY OF RECENT ARTICLES ON ACUTE APPENDICITIS IN CHILDHOOD

Source	Acute Deaths per cent			Abscess Deaths per cent			Peritonitis Deaths per cent			Remarks
	31.4	7	2.2	15.4	4	2.59	14.4	25	17.4	
Allen, P. D. 1937							34	5	14.7	Immediate operation. Mortality (1-5 yrs.) 15.2% 95% right rectus incision. 19 of the deaths occurred within 48 hrs. after operation
Angel, F. et al. 1937	70	0	0				26	7	29.0	99% McBurney incision
Jones, R. Jr. Menejee, E. E. 1937	67	0	0	31	2	6.4	75	9	12.0	All McBurney incisions. Mortality 15 times their adult series
Deaver, J. M. Martin, A. 1938	146	0	0	14	1	7.1	67	4	6.0	Progressively more McBurney incisions. Mortality 1-5 yr. 21.7%. Expectant treatment rarely used
Caldwell, E. 1938	103	1	0.97	50	1	2.0	217	21	9.6	5 of 6 deaths within 30 hrs. of operation. No expectant treatment. 210 McBurney; 10 right rectus
Hudson, H. W. Chamberlain, J. W. 1939	466	2	0.42	156	3	1.9	123	9	7.3	Appendix removed in 95% of cases. 39 McBurney; 797 right rectus incisions. Mortality under 4 yrs. 13%. Immediate operation
Bruce, G. 1939	320	0	0	24	0	0	32	9	28.0	Expectant treatment in only 3 cases. McBurney and paramedian incisions equally used
Edberg, E. 1939	65	1	1.5	83	4	4.7	135	4	2.9	These cases are age group 0-5 yrs. In 1638 cases 0-15 yrs. there were 38 deaths (2.31%)
Gatch, W. D. et al. 1940	521	0	0	?			306	56	18.5	Loss of protein explains "toxemia" of peritonitis. McBurney incision. 119 immediate operation; 16 expectant treatment
Miller, E. M. et al. 1940	629	0	0	228	7	3.1	1159	140	12.8	McBurney incision. "Immediate" operation except in the abscess group
Total	2701	11	0.41	740	22	2.9				

Age. The age distribution is shown in Chart 1. This follows the curve of previously reported series. The age incidence of perforation is strikingly shown. Among all the patients with acute appendicitis, 35.4 per cent had perforation. Between the ages of 1 and 5 years, the incidence of perforation was 71.7 per cent.

Diagnosis. Perforation of the appendix without doubt increases the possibility of a fatal termination, and establishes the certainty of a prolonged morbidity. Although adequate medical and surgical care can do much to improve the final result, we believe that early diagnosis is the most important single factor in the control of this disease.

TABLE II.—ACUTE APPENDICITIS  
Babies' Hospital, New York, 1935-1940 (July)

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Babies' Hospital, New York, 1935-1940 (July

Acute appendicitis without perforation (64.6%)					Acute appendicitis with perforation (35.4%)					Deaths	Total Cases	Total Deaths
Year	Acute	Acute with positive culture	Gangrene	Deaths	Abscess	Local	Spreading peritonitis	General				
Private	27	1	8	0	0	3	1	0	0	40	0	
1935	18	4	6	0	5	6	5	0	0	44	0	
1936	26	1	3	0	5	10	3	1	0	49	0	
1937	17	0	3	0	9	8	3	3	0	43	2	
1938	20	6	5	0	4	11	5	2	0	62	0	
1939	27	4	0	0	7	4	4	0	0	53	0	
1940 (6 months)	16	4	0	0	33	50	23	10	2	326	2	
Totals	160	20	30	0	0	33	50	23	10	326	2	
Grand totals				210	(0.05%)			116	2	(1.75%)	(0.61%)	



# SURGERY, GYNECOLOGY AND OBSTETRICS

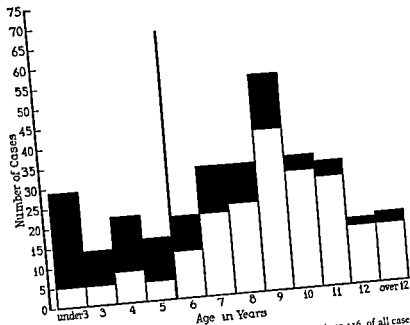


Chart 1. Age distribution of the patients of 5 years of age and younger 71.7 per cent had perforations. White areas, acute appendicitis; shaded areas, perforated appendicitis. Thirty five and four tenths per cent, or 116, of all cases were perforated.

The significance of this is shown in Charts 2 and 3. Only 13 per cent of patients with perforation were seen in the first 24 hours of their disease, whereas nearly 60 per cent of those without perforation were seen during that interval. No patient with appendiceal abscess was hospitalized before the second day of the disease. Some of the factors which may contribute to this delay have been analyzed.

The large proportion of ruptured appendices in patients under the age of 5 years has already been shown in Chart 1. Obviously, difficulties in the accurate communication of symptoms from these patients and the difficulty in evaluating the early physical signs account in part for these high figures. However, we feel that the failure of parents to realize that acute appendicitis may occur in the very young is of greater importance. We cannot emphasize too strongly that episodes which are commonly attributed to "gastro-intestinal upsets" may, in reality, be acute appendicitis. Parental education in this matter has been sadly overlooked.

Catharsis is also related to the all important question of delay in diagnosis. For a number of years it has been stressed that such medication favors the chances of perforation. Bower noted that in patients receiving cathartics 1 in 7 were perforated as opposed to 1 in 80 of the undosed patients. Seventy-three patients in our group received some form of catharsis. Of these 32 were perforated, 41 were not. However, only 1 of the perforated cases was seen in the first 24 hours as against 14 of those with simple acute appendicitis. Of the unperforated cases 6 patients waited 36 hours before coming to the hospital, whereas 15 of the perforated group were first seen after 48 hours of the disease. We do not condone the use of catharsis but would emphasize that the delay associated with the administration of such drugs is of the greater importance.

Despite the policy of this clinic regarding immediate operation, 26 patients with proved acute appendicitis were not operated upon the day of admission. Seventeen of these were in the nonperforated group and fortunately in

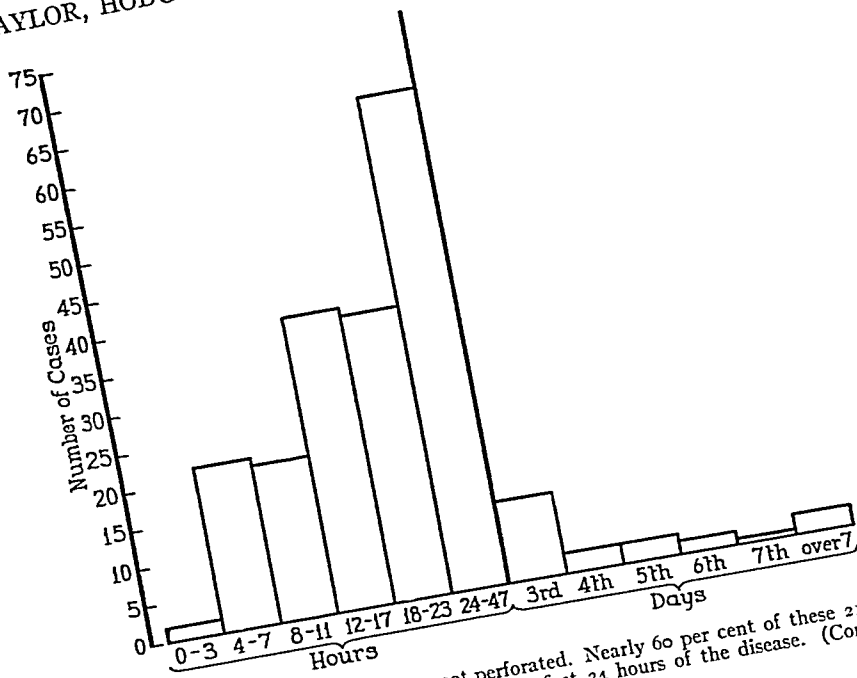


Chart 2. Duration of symptoms, not perforated. Nearly 60 per cent of these 210 cases without perforation were seen within the first 24 hours of the disease. (Compare with Chart 3.)

only 1 case was there an increased morbidity. Of the 9 perforated cases, 4 were purposely delayed and will be discussed further. In 3 others the history of recent abdominal trauma was misleading and they were observed for 24 hours. In the 2 remaining the diagnosis was missed and the delay in operating undoubtedly increased the morbidity in these patients and accounted for their long and complicated postoperative courses.

The history, the temperature, the white blood count, and the physical examination are points which bear on the recognition of the disease and on the estimation of the degree to which the process has progressed.

Most patients had a characteristic history consisting of abdominal pain, fever, and vomiting. In the great majority the pain preceded the vomiting. The duration of the disease is usually brief, since 79 per cent were seen and diagnosed within 48 hours of the onset of symptoms. Most patients had had no previous episodes of similar abdominal pain. Colic-like or cramp-like pain was noted in

many instances. In these an inflamed pelvic or midline appendix was frequently found lying among the coils of the ileum. Diarrhea, which often is used as an argument against the presence of acute appendicitis, was encountered in 20 cases.

The preoperative complications were upper respiratory infection, 6 without, 17 with perforation; acute otitis media, 1 without, 1 with perforation; bronchitis, 1 with perforation; bronchiectasis, 1 with perforation; pulmonary tuberculosis, 1 without perforation; genitourinary malformation, 3 without, 2 with perforation; symptoms of infection of genitourinary tract, 4 without, 8 with perforation; vaginitis, 2 without, 1 with perforation; exacerbation of previously drained appendicitis, 3 without, 5 with perforation; abdominal trauma, 1 without, 4 with perforation; exanthemas, 2 without, 1 with perforation; rheumatic fever, 1 without perforation; chronic glomerular nephritis, 1 without perforation; tuberculous cervical adenitis, 1 with perforation; fistula-in-ano, 1 without perforation.

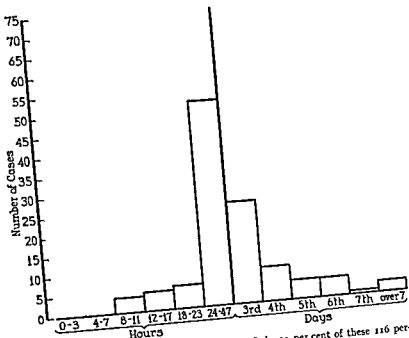


Chart 3 Duration of symptoms, perforated. Only 13 per cent of these 116 perforated cases came to the hospital during their first 24 hours of illness

From this we conclude that the presence of other known disease, notably upper respiratory infection, should not militate against the diagnosis of acute appendicitis.

Symptoms suggestive of urinary tract disease may be confusing. At least 12 patients complained of frequency or pain on urination. The majority of these were found to have an acutely inflamed appendix lying in proximity to the bladder.

The admission temperatures are analyzed in Charts 4 and 5. Eighty-six per cent of patients with simple acute appendicitis had readings below 102 degrees F. In a suspected case when the temperature is greater than 102 degrees, without other obvious cause, it is likely that simple appendicitis is not present. In no instance was a shaking chill noted. This is despite the fact that many of the children were severely ill and is in contradistinction to the findings in a like group of adult patients.

Charts 6 and 7 demonstrate that little reliance as a differential point can be placed on the leucocyte count alone. The curves for patients with simple acute appendicitis and

for those with perforation overlap widely. The frequency curve for suspected cases, in which normal appendices were found, similarly overlaps.

The findings at physical examination varied. However, all patients showed some degree of localized abdominal tenderness. Rectal tenderness or rebound tenderness, increased resistance of the rectus muscles, or a combination of these signs were also usually present. The intensity of these depended greatly on the emotional state of the individual child. All these findings, physical and laboratory, were often extremely unreliable as indices of the true degree of peritoneal involvement. This disparity between preoperative impressions and actual findings at operation is another reason why we never institute expectant treatment on the basis of a preconceived idea of the extent of the pathological process.

**Operation** It is the policy of this clinic to operate immediately on all patients in whom a diagnosis has been made of acute appendicitis. To this rule there are two possible exceptions. In children who are seriously ill, sufficient

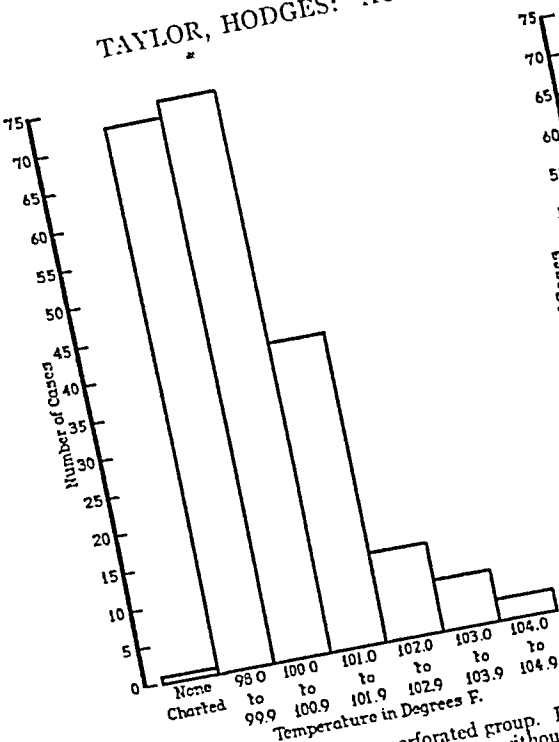


Chart 4. Temperature in nonperforated group. It will be seen that 86 per cent of these patients without perforation had temperature readings below 102 degrees F.

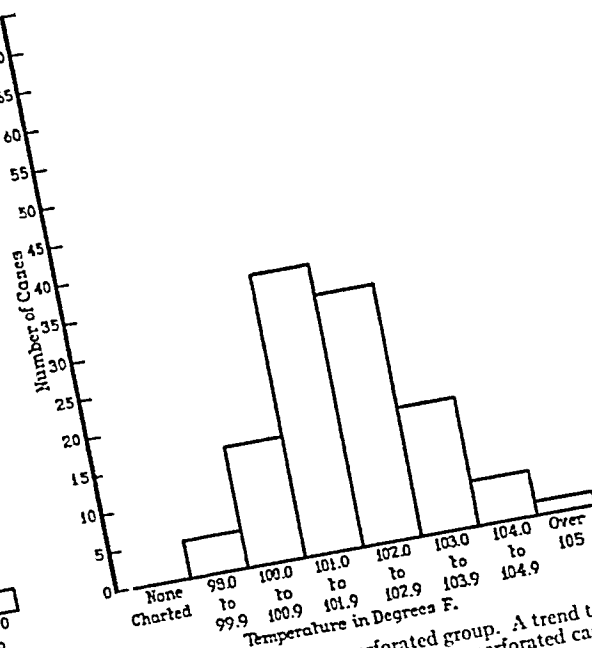


Chart 5. Temperature in perforated group. A trend to a higher temperature range is seen in these perforated cases, but no significant deductions may be drawn.

time is allowed to correct their dehydration, acidosis, and serum protein deficit by appropriate means. The second exception is made, at times, in patients with clear-cut appendiceal abscesses which have probably been present for about 5 days. Such cases will be discussed. This practice of prompt operation is in agreement with the views already expressed—that the mortality and the morbidity are in direct proportion to the time interval allowed to elapse between the onset of symptoms and the operation. We believe that our figures show that there is no advantage in the Ochsner plan of delayed operation even in the advanced cases.

Inhalation anesthesia was used almost exclusively, open ether being given to the great majority. This was felt to be a safe and satisfactory anesthesia to administer in this age group. The postoperative complications of inhalation anesthesia seen in the older age groups were almost never observed in these children. In the last year or two, atropine or scopolamine, with or without nembutal or

seconal, have been used with increasing frequency as adjuncts to etherization. It is felt that these drugs promote a smoother course of anesthesia.

Save for a few private patients, the operations were distributed among a group of 10 surgeons.

The McBurney incision was used in all but 11 of the patients. In 6 of these exceptions there was a definite indication, such as a preoperative diagnosis of ruptured viscus or volvulus or a midline mass. We strongly advocate the McBurney approach, since we feel that it has contributed greatly to the low mortality and to a reduced morbidity, especially in the contaminated cases. We agree with Allen's opinion that, in patients with a perforated appendix, better results are obtained if little but the peritoneum is approximated around the drains. This would be a distinctly hazardous procedure in a right rectus incision. In delivering the appendix through a rectus incision, considerably more handling and packing off of the intestine is

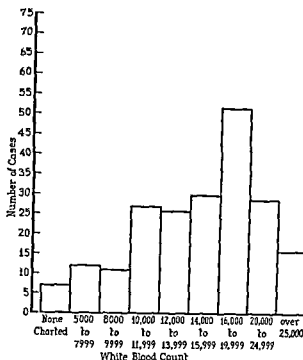


Chart 6 Leucocyte count in nonperforated group. The leucocyte counts in the cases without perforation cover a relatively wide range.

necessary than is required in the intermuscular approach. Furthermore, when drainage is instituted through a right rectus incision, the chance of intestinal obstruction is increased, for a larger surface of ileum tends to be in contact with the drains. In the excellent paper of Hudson and Chamberlain from the Children's Hospital of Boston, a right rectus incision was used in 94 per cent of 839 cases. They have listed intestinal obstruction as a postoperative complication in 20 cases, and 10 of these required a secondary operation. We have encountered moderately severe ileus in 15 patients of our series. Of these, only 3 were considered to be on a mechanical basis and in no instance was a secondary operation for obstruction required. The only instance of wound disruption in our series was in a patient operated upon through a right rectus incision. The majority of authors (Table I) share our advocacy of a McBurney incision. Bruce found little to choose between the two procedures.

The appendix was removed in all the non-perforated cases. In the patients with perforated appendices, the organ was removed save in the instances in which the operator deemed that such a procedure entailed too much manipulation with further peritoneal soiling. There were 13 of these cases. In all of these the appendix was subsequently removed. Five of these were removed during a second acute episode which required immediate operation. This emphasizes the great importance of subsequent appendectomy in those cases in which only drainage is performed at the first operation. Although in 4 of these the delay was the result of lack of parental co-operation, in the fifth the incident occurred within the prescribed "waiting period." We have, therefore, shortened this "waiting period" to 4 or 5 weeks after discharge.

The selection of those patients in which drainage should be employed is often difficult. On one hand there is the group of simple acute

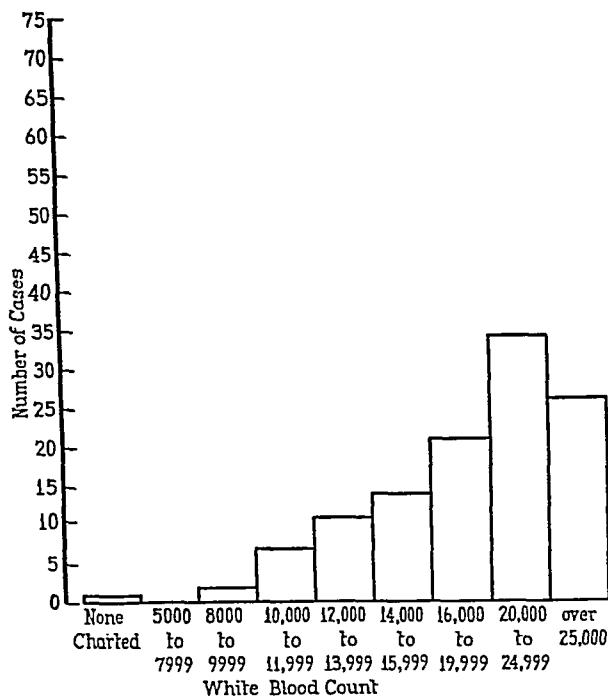


Chart 7. Leucocyte count in perforated group. Although more very high leucocyte counts are noted in the perforated cases, the distribution overlaps those in Chart 6.

appendices in which drainage is not indicated, on the other, the cases with large abscesses which clearly should be drained and between these fall a fairly large number of debatable cases. We have attempted to estimate the advantages of drainage in this middle group, using morbidity as our chief criterion.

Twenty of the nonperforated cases were drained. In 3 of these the appendix was ruptured during removal, in 2 there was a question of perforation. In one instance, considerable induration of the cecum was found in a patient operated upon for an acute flare-up of a recently drained appendiceal abscess. Seven patients had friable retrocecal appendices, requiring dissection during their removal, and were drained. In the 7 remaining, the reason for drainage was not stated. Only 3 of these drained, nonperforated cases were ready for discharge at the expected time, the tenth postoperative day (Chart 8). On the other hand, cultures of the peritoneal cavity, taken at operation, were positive in 25

nonperforated cases. Only 3 of these were drained and there were no complications. Furthermore, 8 of the perforated cases were closed without drainage. Only 1 of these developed a complication, a pelvic abscess which responded to conservative treatment. We feel, therefore, that drainage should be withheld in all nonperforated cases unless there has been unusual tissue damage or gross break in technique. Further a number of cases with early, well localized perforation can be closed primarily without endangering the patient. The judgment of the experienced operator as regards this question of drainage will appreciably and safely decrease the morbidity. Blind adherence to the maxim "when in doubt drain" is to be condemned.

When drainage is indicated, the simplest possible type is used. It is felt that by placing the drains in minimum contact with the bowel and by giving special attention to the pelvis and the lumbar gutter, maximal results can be obtained. In the badly contaminated cases

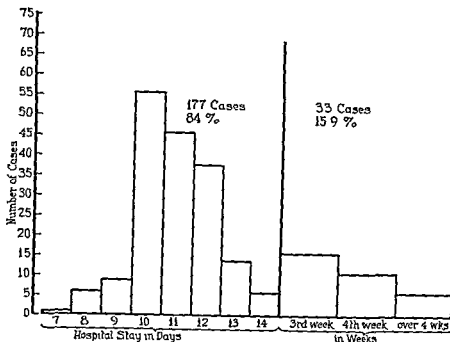


Chart 8 Of the 33 cases that remained in hospital longer than 2 weeks, 9 were drained, 10 had wound complications, 1 developed a pelvic abscess, and in 4 no reason was apparent. The 9 other patients had conditions unrelated to the operation.

loose or no closure of any layer but the peritoneum only was employed. This procedure is known to lessen the extent of wound infection and incidence of postoperative herniation (1).

**Treatment** In the seriously ill patients, fluid, electrolytes, and blood were given as promptly as possible in order to prepare the patients for early operation. This is an integral part of the policy of "immediate" operation.

The need for postoperative parenteral fluids varied widely. A large group of patients with simple acute appendicitis and early operation were given no parenteral fluids. These patients showed remarkably little reaction to the operative procedure and were able to take adequate fluids by mouth shortly after their return to consciousness. However, many of the children, especially those in the younger age groups, were affected by their disease and by their operation. One indication of the frequency of this metabolic upset was the presence of three or four-plus acetone in the

admission urine of 33 per cent (111) of the patients. These were treated after operation with subcutaneous or intravenous fluids in amounts proportional to their body weight. In children with widespread infections and prospects of ileus, infusion by constant intravenous drip regularly was used. The amounts were regulated by the weight of the child, by clinical evidences of dehydration, and by the quantity of fluid obtained by gastric siphonage when that form of therapy was used. Sodium lactate or saline lactate were used in those patients showing clinically or chemically determined evidence of acidosis. Electrolyte solutions were frequently supplemented by plasma (11) when hypoproteinemia was present or expected. This was given through the intravenous drip and was supported by glucose solution when there was prospect of prolonged starvation. Whole blood was administered by separate injection, since the intravenous drips in these children must be run so slowly that clogging, due to sedimentation of the red blood cells, often occurs.

All these therapeutic procedures were prescribed and administered by members of the pediatric interne and resident staffs. These were in constant attendance on the Surgical ward and were thus able to apply their experience in fluid administration in children to these postoperative patients.

In the treatment of postoperative abdominal distention, we have used a Levine tube together with constant siphonage by the method of Wangenstein. This has given satisfactory results. In those patients with extensive peritoneal contamination we have tried to anticipate the expected distention by instituting gastric siphonage immediately after operation. Almost all the patients tolerated this well. By this procedure, we feel that we have frequently avoided the severe distention which would otherwise have occurred on the second or third postoperative day. Attempts to pass a Miller-Abbott tube have so far been almost uniformly unsuccessful in this group of children. We have had no experience with the use of high concentrations of oxygen in the treatment of distention (10).

With the increasing use of chemotherapeutic agents in infections it is natural that they should be applied to peritonitis. In view of their known success in treating infections of the urinary tract by the colon bacillus group of organisms, they have been hopefully applied to peritonitis of appendiceal origin. Favorable experimental and clinical results have been reported. We have employed chemotherapy in 17 unselected cases of peritonitis during the last year and one-half and have found no conclusive evidence of its benefit.

Since the mortality in this series has been almost nil, we have been obliged to resort to other criteria in order to judge the effect of sulfanilamide and its derivatives. One of these is the clinical impression. In the treated group several patients showed a prompt drop in temperature and an early symptomatic improvement. A corresponding number showed no such evidence of benefit. A large proportion of the untreated group showed a similar rapid postoperative improvement. A more accurate criterion was the duration of hospital stay. Six patients with localized peritonitis

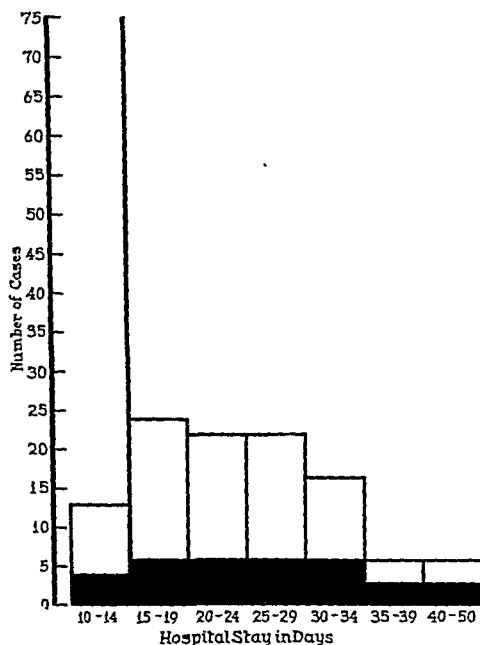


Chart 9. Hospital stay, perforated group. Three patients remained less than 10 days (1 transferred for measles, 1 death, 1 improved; discharged for subsequent operation). Four remained longer than 50 days—(52, 81, 95, 105). White areas, peritonitis cases; black areas, abscess.

received chemotherapy immediately after operation for from 4 to 14 days. None developed major intraperitoneal complications. The duration of their hospital stays were 11, 14, 15, 24, 26, and 32 days. Three patients with diffuse peritonitis received similar treatment. One did well, developed no major complications, and was discharged on the twenty-third day after operation. The 2 others developed pelvic abscesses and remained in the hospital 37 and 43 days, respectively. Two localized abscesses were treated before operation. These patients were not discharged until the 34th and 45th day. Three postoperative abscesses were treated without demonstrable effect. Their respective morbidity was 21, 33, and 39 days.

A number of treated patients showed marked irritability or mental confusion which amounted, in several instances, to frank delirium. One child had a severe hemolytic crisis while already in a seriously ill condition.

Comparing the durations of hospital stay of the treated cases noted with the stays of



those who went untreated, no significant difference is found (Chart 9). When the weight of the complications of chemotherapy is added to this, we feel that we have no good evidence of its advantage in appendiceal peritonitis. It is possible that the drugs may have a use as a protective agent in very early rapidly spreading peritonitis.

*Treatment of appendiceal abscesses.* The treatment of appendiceal abscess is a controversial subject (7). It is in this group that delayed operation has been most often recommended. In judging our results we have used duration of hospital stay as the chief criterion, as there has been no mortality under either regimen.

Seven of the 33 patients in this group were treated expectantly. Two had to be operated upon during their hospital stay and had long postoperative courses. In neither could the appendix be removed. Three patients were given chemotherapy and were discharged improved after 9, 25, and 35 days, respectively. On readmission for "interval" appendectomy, they remained 25, 30, and 35 days, and all required drainage. Two patients did well with delayed operation. The average hospital stay of these patients was longer than that of the rest of the group who were operated upon promptly. From a purely statistical point of view in this small series, it would seem that little was to be gained from postponing surgical intervention in appendiceal abscesses. However, we do feel that there are cases with localized signs, mass, and a history of 5 days or more that do better if observed. Such observation should be carried out in the hospital under the close scrutiny of the surgeon in charge. If no improvement is evident within 12 to 24 hours, operation may be performed without any added risk to child. On the other hand at times an unnecessary and possibly damaging operation can be avoided. All these patients should subsequently have interval appendectomies.

*Complications.* Secondary intraperitoneal abscess formation was the most frequent postoperative complication, occurring 29 times. Twenty-two of these had pelvic collections as evidenced by fever, leucocytosis, palpable mass, and a subsequent evacuation of large

amounts of pus by bowel or through the operative wound. Five patients formed more than one abscess in the lower abdomen. None of these patients were operated upon for this complication. All recovered. In most it was necessary to resume, during their stage of greatest illness, the supportive measures which have been described under postoperative treatment, paying particular attention to the serum protein. We feel that a conservative attitude toward this type of secondary abscess is of great importance. Although several of these children became very ill, all recovered without undergoing the added danger of operative intervention.

Four patients developed subphrenic or subhepatic collections of pus. None of these responded to conservative treatment, probably because of the more unfavorable anatomic locations of the suppurative process, and all were operated upon, with 1 death. Secondary operations were performed on 5 other patients, once for suture of an eviscerated right rectus incision, once for costal drainage of empyema, and three times for the drainage of wound infections.

*Operations for acute appendicitis.* Normal appendices found. During the same  $5\frac{1}{2}$  year period 60 patients in whom the appendices were histologically normal were operated upon as emergencies with the preoperative diagnosis of acute appendicitis. A review of these cases is included in order to give this study a fuller perspective. They may be divided into 4 groups: those in whom no explanation for the symptoms was found (16), those in whom various pathological conditions were found to account for the symptoms (17), those with mesenteric adenitis (24), and those with primary peritonitis (3).

The cases in which no organic lesions were found represent a margin of error in the attempt at early diagnosis and treatment of acute appendicitis. All were in age groups in which the disease is most frequently suspected (all were 6 years of age or more). Although, as we have mentioned, recurrent attacks of abdominal pain were rare in true appendicitis, 11 of these 16 had a history of such attacks. The decision to operate in many of these was influenced by a natural desire to be rid of the

disquieting uncertainty caused by these repeated episodes. Only 3 patients had classifiable preoperative findings of acute appendicitis.

Acute mesenteric adenitis is frequently indistinguishable before operation from acute appendicitis. Analysis of our 24 cases showed no diagnostic points by which the two diseases could be differentiated. Eleven had pain without vomiting, a relatively infrequent finding in true appendicitis. It often has been expressed that mesenteric adenitis is frequently associated with upper respiratory infection. Only 2 of this group gave a recent history of such a condition.

Primary peritonitis may be extremely difficult to distinguish from peritonitis of appendiceal origin. This is especially true in very young patients. In 3 patients this diagnostic error was made, the organism in all being the pneumococcus. All of these were seen before July, 1937. Since that time we have made increasing use of diagnostic peritoneal puncture. So far this has given conclusive information in all instances in which it has been used, making the diagnosis of appendicitis in three instances. It is conceivable that some cases of very early primary peritonitis will show no organisms in the smears from the paracentesis, under which condition operation may be indicated. This is apparently a safe procedure, for in certain other clinics (16) this diagnosis is regularly confirmed by abdominal incision.

None of these 60 patients showed any untoward effects from the operative procedure. Approximately, then, for every 6 cases of true appendicitis, one normal appendix has been removed (1 in 10 if the cases of mesenteric adenitis are excluded). Although this figure could doubtless be improved, we regard it as a justifiable margin of error in the effort to diagnose and operate upon this disease at the earliest moment possible. We would prefer to remove several normal appendices if by that means we may prevent a perforation in a patient who is being observed due to diagnostic difficulties. We feel that our mortality figures bear out this view.

*Morbidity and mortality.* The patients with acute appendicitis without perforation are usually discharged sometime during the sec-

ond hospital week. As can be seen from Chart 8, approximately 50 per cent are sent home on the 10th or 11th postoperative day. Arbitrarily all the patients staying after the 14th day were considered to have an increased morbidity. There were 33, or 15.9 per cent, that stayed into the third week or longer (Chart 8).

No standard could be established for the perforated cases as regards morbidity. The hospital stay of these patients is plotted in Chart 9 for statistical purposes. In all but 6 cases the length of stay was directly dependent upon the number and severity of the peritoneal complications.

The mortality for the entire series is 0.61 per cent, or 2 deaths in 326 patients. This figure must be interpreted in the realization of the fact that the deaths from acute appendicitis without perforation are negligible as evidenced by reports from various clinics. In 2,701 such cases collected in Table I the mortality was 0.04 per cent. In our series there were no deaths in 210 cases without perforation. The mortality problems, therefore, are virtually limited to the perforated cases. There were 116 cases in this group with a mortality of 1.75 per cent. This also should be further broken down, for among the cases with perforation are those with localization or abscess formation, and these have in general been shown to have a mortality of only 0 to 2.5 per cent with thoughtful treatment. There was no mortality in this type of case in the present series. The 2 deaths occurred among the 33 remaining cases, those that had no evidence of localization at operation and were considered to have spread beyond the right lower quadrant. The mortality rate in this subgroup is, thus, 6.06 per cent, a result which shows a marked improvement over the previous 5 year period at this hospital, and which compares favorably with the best reported adult series.

It was particularly gratifying to find that of 81 patients of 5 years or under, 71.7 per cent of whom had perforated appendices, there was but 1 death, 1.22 per cent. This patient was 22 months of age and his case was the only death in 29 children under the age of 3 years.

## SUMMARY

We feel that the factors that influence the mortality and morbidity rate in acute appendicitis in children are in order of their importance: (1) duration of symptoms before operation; (2) the type of operative treatment, which includes that given in the immediate preoperative period; (3) the type of postoperative care and treatment, and (4) the age of the patient.

It appears from the data presented that there is nothing inherent in acute appendicitis in children that should necessitate higher mortality and morbidity rates than in adults. Difficulties in obtaining the history or in the interpretation of early physical findings in infants, and anatomical considerations such as the small short omentum and the thinness of the wall of the intestine, will always add to the difficulties of diagnosis and the hazard of the disease in the younger age groups. However, the absence of serious concomitant disease in children, particularly of the chronic type, offsets these considerations. The great recuperative powers and the resiliency of the organically sound child when receiving adequate supportive treatment makes the prognosis better than in the adult with the same extent of disease.

It is believed that the low mortality figures in the series presented are dependent on the combination of several factors employed in the management of these children:

1. Immediate operation, but with the patient fully prepared before operation as far as water, electrolyte, and protein balance are concerned.

2. Routine use of the McBurney incision.

3. Simple incision and drainage if removal of the appendix entails the danger of further spreading the disease process.

4. Parenteral fluids following operation, continuously if necessary, to satisfy the unusual demands.

5. Free use of whole blood and plasma intravenously to combat the protein losses in

the presence of extensive peritoneal involvement and secondary abscess formation.

6. Indwelling Levine tube with constant Wangenstein suction not only in the presence of ileus but in anticipation of it.

7. A nonoperative, conservative attitude toward secondary abscesses in the lower abdomen.

Although chemotherapy is of great value in the treatment of complications unrelated to the disease, e.g., pneumonia, we have little evidence of its benefit in peritonitis of appendiceal origin.

In order to give a true perspective to this series, the 60 patients who were operated upon during this same period for presumed acute appendicitis, but were found to have normal appendices, have been reviewed.

We wish to express our sincere appreciation to Dr. Edward J. Donovan on whose teaching and guidance the management of these cases has been based, and to Dr. Rustin McIntosh for his helpful criticism in the preparation of the text, also to the surgical nursing staff of the Babies' Hospital whose thoughtful care has played such an important part in the favorable results in many of these patients.

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# BENEFICIAL ACTION OF OXYGEN THERAPY

## EXPERIMENTAL SHOCK

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A REVIEW of the theoretical basis for the use of oxygen in the treatment of shock was reported in an earlier paper (4). In addition the recent experimental evidence of Wood, Mason, and Blalock showed that following the development of mild experimental shock in dogs, inhalation of a high concentration of oxygen for only 15 minutes had a beneficial action. The average blood pressure was elevated 6 and 7 millimeters of mercury in the dogs in which shock was produced by repeated hemorrhage and by repeated subcutaneous injections of small doses of histamine. No effect was observed upon the blood pressure in their dogs in traumatic shock. In all groups the oxygen therapy caused a decreased pulse, increased respiration, and an increased oxygen content of the arterial and venous blood. Our more extensive studies on traumatic shock showed that oxygen therapy had a definite beneficial action upon the blood pressure and the length of life of the dogs. Of two groups of dogs with an average similar amount of trauma and fluid loss into an injured limb, the group of dogs which was treated with oxygen did not show such a marked fall in blood pressure 4, 6, and 8 hours after injury and lived 70.3 per cent longer than the untreated group. The oxygen content of the arterial and venous blood was also increased by oxygen therapy in our dogs.

This paper reports the results of our studies upon the effects of inhalation of a high oxygen concentration upon peripheral circulatory failure produced by slow intravenous injection of histamine. The report of Wood, Mason, and Blalock contains the results of only 7 experiments in which shock was produced by subcutaneous injections of small doses of histamine. In addition they present only one

observation in each case after 15 minutes of oxygen therapy. They stated that their results were less consistent because their method made it difficult to control the degree of shock due to fluctuation of the blood pressure in their dogs. For this reason we have made more extensive studies with a method which makes it possible to reproduce similar depressions of blood pressure with very little fluctuation.

### METHODS

Twenty normal dogs in a fasting, basal condition were used in the first part of this study. Only the initial intravenous injection of sodium pentobarbital (25 to 30 mgm. per kilogram of body weight) was necessary to maintain anesthesia throughout the experiment. A kymographic record of the blood pressure was made by a mercury manometer attached to the left carotid artery by a cannula. Respirations were recorded by means of tracings of the chest movements. Hematocrit determinations by the capillary tube method were made every 2 hours upon samples of oxalated blood taken from an exposed right femoral vein. The left femoral vein was cannulated and attached to a Murphy drip. By a constant slow drip administration of histamine acid phosphate in physiological sodium chloride solution (0.5 mgm. per c.cm.), any degree of shock without marked fluctuations in the blood pressure could be maintained over a long period of time and reproduced in all of the dogs. A fatal level of blood pressure of 40 millimeters of mercury was maintained in all of our experiments. The duration of life was noted. Ten of the dogs served as controls and breathed atmospheric air (21 per cent oxygen). Continuous 100 per cent oxygen was administered to the 10 treated dogs by a Heidbrink gas machine attached to a cannula in the trachea.

The effect of different oxygen tensions (10, 15, 20 and 95 per cent) in the inspired air

From the Hixon Laboratory of Experimental Medicine and the Department of Surgery, University of Kansas School of Medicine.

TABLE I.—LENGTH OF LIFE OF NEMBUTALIZED DOGS IN CONTINUOUS HISTAMINE SHOCK BREATHING ATMOSPHERIC OXYGEN<sup>1</sup>

Dog	Blood pressure mm mercury		Hematocrit		Length of life Hours
	Initial	Histamine shock	Initial	Histamine shock	
1	130	40	47	65	3.6
2	140	40	41	62	9.2
3	175	40	45	64	3.1
4	140	40	39	48	10.0
5	130	40	52	66	1.7
6	150	40	37	51	9.7
7	130	40	43		1.5
8	150	40	55	80	7.1
9	150	40	45	58	11.7
10	160	40	56	61	6.0
Average	145.5	40	45.8	61.5	5.67

<sup>1</sup>(Almost 21 per cent oxygen)

upon the speed of recovery from histamine shock was studied in 3 dogs. Single intravenous injections of 0.15 and 0.25 milligram of histamine were used to produce the fall in blood pressure.

#### RESULTS

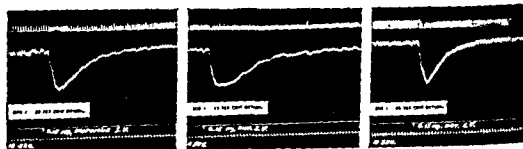
The results upon the control group of 10 dogs breathing atmospheric air (21 per cent oxygen) are presented in Table I. The histamine depressed the average initial blood pressure of 145 millimeters of mercury to the shock level of 40 millimeters of mercury. This pressure was maintained without much variation for the duration of the experiment until just before death. The shock resulted in hemoconcentration. The average hematocrit in-

TABLE II.—EFFECT OF 100 PER CENT INHALATIONS UPON THE LENGTH OF LIFE OF NEMBUTALIZED DOGS IN CONTINUOUS HISTAMINE SHOCK

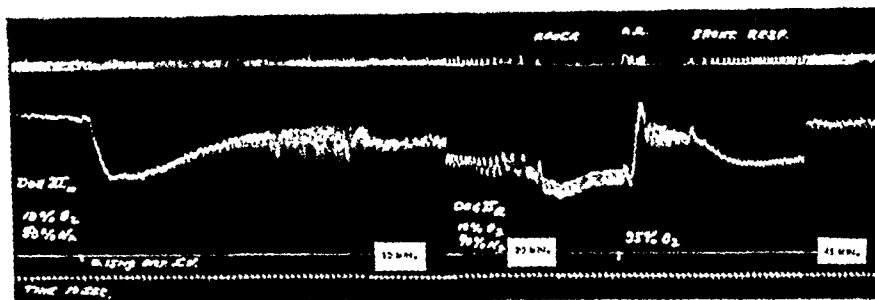
Dog	Blood pressure mm mercury		Hematocrit		Length of life Hours
	Initial	Histamine shock	Initial	Histamine shock	
1	170	40	46	58	15.5
2	90	40	45	62	8.0
3	120	40	41	55	8.5
4	140	40	44	51	11.1
5	115	40	46	65	3.6
6	126	40	51	57.7	12.3
7	150	40	51	59	17.0
8	130	40	45	70	3.6
9	150	40	44	83	8.7
10	120	40	49	63	10.5
Average	127.7	40	45.3	62.1	9.84

creased from 45.8 to 61.5 per cent. This is a 15.7 per cent increase. The length of life varied from 1.5 to 11.7 hours, with an average duration of 5.67 hours.

The effects of inhalation of 100 per cent oxygen are presented in Table II. The histamine decreased the average blood pressure from 127.7 to 40 millimeters of mercury. Hemoconcentration increased the average hematocrit from 45.3 to 62.1 indicating a 16.9 per cent increase. The length of life varied from 3.6 to 17.0 hours, with an average of 9.84 hours. This represents an average increase of 71.7 per cent in length of life of dogs treated with 100 per cent oxygen as compared with that of dogs breathing atmospheric oxygen.



Graph 1. Blood pressure response to the intravenous injection of 0.15 milligram of histamine in the nembutalized dog inhaling 20, 15, and 0 per cent oxygen.



Graph 2. Secondary anoxic shock following the intravenous injection of 0.15 milligrams of histamine in the nembutalized dog breathing 10 per cent oxygen. Recovery after brief artificial respiration and 95 per cent oxygen.

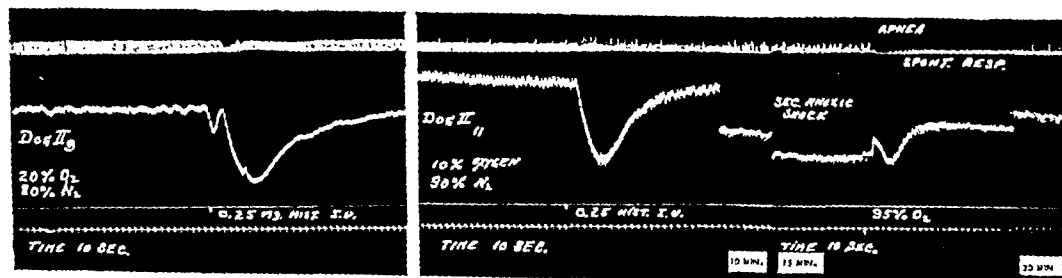
Postmortem examination showed moderate vasodilatation in the intestines. The liver was red and apparently normal in size. This contrasted with the anemic appearance of the intestines and viscera found in dogs dying from traumatic shock.

Repeated intravenous injections of small doses of histamine acid phosphate (0.15 and 0.25 mgm.) produced almost identical depressions in the blood pressure in the same dog. Experiments upon three nembutalized dogs showed that the rate of recovery of the blood pressure after such an injection was decreased if the animal breathed 15 per cent oxygen instead of 21 per cent oxygen. This is shown in Graph 1. When the dogs were given 100 per cent oxygen the rate of recovery of the blood pressure was again normal. When only 10 per cent oxygen was inhaled the initial fall in blood pressure was followed by slow recovery to a level below normal and after 15 to 20 minutes a secondary depression of blood pressure occurred. The initial fall in blood pressure was accompanied by a reflex slowing in the respira-

tion. Slow restoration of the blood pressure from secondary anoxic shock could be produced by the administration of 95 per cent oxygen as shown in Graphs 2 and 3.

#### EVALUATION

The slow intravenous drip injection of histamine produced a continuous depression of blood pressure which did not vary much and which was duplicated in a series of dogs. Because of this, it is an excellent method for studying the effect of oxygen therapy upon peripheral circulatory failure. The clinical analogue occurs in anaphylactic shock. Dragstedt and Gebauer-Fueluegg (1) have reported finding histamine, or a histamine-like substance, in the blood and lymph of dogs during anaphylactic shock. The amount was proportional to the severity of the shock. Histamine of similar vasodepressor substances apparently not involved in traumatic shock. Dragstedt and Mead (2) failed to find a vasodepressor "toxin" in the blood and lymph of dogs during experimental traumatic shock. The use of



Graph 3. Secondary anoxic shock following the intravenous injection of 0.25 milligrams of histamine in a nembutalized dog breathing 10 per cent oxygen. Spontaneous recovery following the administration of 95 per cent oxygen.

## SURGERY, GYNECOLOGY AND OBSTETRICS

oxygen therapy in peripheral circulatory failure produced by histamine is logical in view of the depressed oxygen content of the arterial and venous blood of dogs in histamine shock reported by Wood, Mason, and Blalock. Their results show that even 15 minutes of pure oxygen inhalations exert a beneficial action. Our results show that continuous oxygen therapy prolonged the life of the dogs by 71.7 per cent. Our results also confirm their report of hemoconcentration in histamine shock.

The experiments with repeated single intravenous injections of 0.15 and 0.25 milligram of histamine demonstrate the rôle that oxygen plays in the normal reactivity of the vasomotor system and capillary tone in maintaining the blood pressure. Inhalations of 15 per cent oxygen slowed the recovery of the vasomotor mechanism and a secondary anoxic fall in blood pressure developed 15 to 20 minutes after incomplete recovery from the first fall. Slow recovery followed the inhalation of 95 per cent oxygen. A depression of the carotid sinus pressor reflex by the anoxemia is undoubtedly involved in these reactions. Gellhorn and Lambert have shown in narcotized dogs that inhalation of 7 and 9 per cent oxygen greatly reduces the pressor reflexes of the carotid sinus. A greater fall in the carotid blood pressure occurred when the position of the dogs who inhaled 7 to 9 per cent oxygen was

changed from horizontal to vertical than when they inhaled 20 per cent oxygen. In addition they reported a diminished response of the blood pressure during anoxemia to a given increase of pressure in the carotid sinus.

## CONCLUSIONS

1. A blood pressure of 40 millimeters of mercury was continuously maintained in 20 nembutalized dogs by the slow intravenous drip injection of histamine.
2. A 15.7 and 16.9 per cent hemoconcentration developed during histamine shock in the 2 groups of dogs studied.
3. Oxygen therapy—100 per cent—prolonged the lives of the treated dogs by 71.7 per cent as compared to the dogs breathing atmospheric oxygen—21 per cent.
4. Anoxemia depressed the capillary tone and the pressor reflex activity of the carotid sinus. This was restored by oxygen therapy.
5. Oxygen inhalation is beneficial in peripheral circulatory failure due to histamine.

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# PAPILLARY ADENOCARCINOMA OF THE KIDNEY

## Hypernephroid Tumors

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THE pathogenesis of epithelial tumors arising in the substance of the kidney has been a matter of dispute for a number of years, particularly since Grawitz introduced the idea that they arise from suprarenal rests caught in the kidney during its development. This idea was enthusiastically accepted, so that all tumors were considered to be "hypernephromas." Stoerk soon threw doubt, however, into the authenticity of this pathogenesis by separating those tumors which showed evidence of tubular and/or papillary formation and by advancing the theory that the latter arise from nephrogenic elements.

The modern tendency is to eliminate the suprarenal genesis and consider the tumors as of nephrogenic origin. It is true that the cells in many of the tumors have the clear, vacuolated appearance that we sometimes see in suprarenal epithelium, and there is the intimate relationship between the cell columns and the thin walled blood vessels, as is normally found in suprarenal tissue. These findings, and the absence of lumina and the papillary feature, led Grawitz to state that they were of suprarenal origin, particularly after he had found suprarenal rests in normal kidneys. A thorough study of the individual tumor, however, will usually show wide variation of histological character, and while the clear cell, the absence of lumina, the intimate relationship with blood vessels may prevail, there will be foci where tubules, papillary arrangement, and granular cells are present.

The most important point in the argument against the suprarenal origin is the lack of evidence of hormone (cortin) activity. The term "hypernephroma," however, has become so thoroughly fixed in the nomenclature of tumors of the kidney that it will be very difficult to eradicate. There is no objection to the use of the term "hypernephroma" if the proper connotation be ascribed to it. The modern term, "hypernephroid," is more accurate but rather bulky.

In spite of the authorities cited, we have not reached the point where we can deny the possibility of a true hypernephroma in the kidney, so at present the classification must be on a rather broad morphological basis.

We speak of a tumor as adenoma, papillary adenoma, adenocarcinoma, papillary adenocarcinoma with clear or granular cells. Whether there is any particularly important clinical significance to this elaborate classification is not known. The solution may be found when the large amount of material in the kidney tumor registry of the American Urological Association is analyzed. It must be remembered that this discussion does not include papillary carcinoma of the kidney pelvis, nor various types of Wilms' tumor, nor the adenocarcinoma of renal blastema.

Lucké stated, "There are many reasons why most pathologists today believe that the so called hypernephromas do not develop from misplaced adrenal tissue, but rather from renal epithelium. Among these reasons are: lack of endocrine disturbance and absence of corticin, the fact that adrenal rests in other parts of the body do not give rise to tumors, the glycogen content in the cytoplasm of cells in hypernephromas (lipoid content in adrenal cells), and the difficulty in understanding why the most common tumor of the kidney would arise from something that does not normally belong to the kidney. All of these facts would indicate that these tumors are true adenocarcinomas."

Read by invitation at the group conference on "Malignancies of the Kidney," Clinical Congress of the American College of Surgeons, Chicago, Illinois, October 25, 1940.  
Dr. Ash, Lt. Col., M. C., U. S. A., Curator Army Medical Museum.



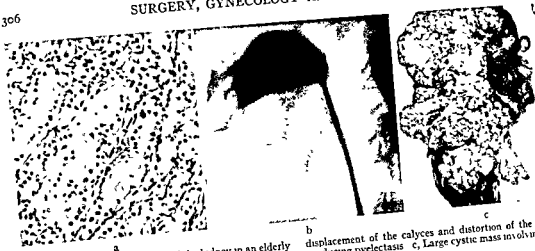


Fig 1 Hypernephroid tumor of the kidney in an elderly male a, High power section showing the tubular formation b, Retrograde pyelogram with marked downward

displacement of the calyces and distortion of the pelvis, producing pyelectasis c, Large cystic mass involving two-thirds of the kidney

Papillary adenocarcinoma is the most common tumor of the kidney and occurs chiefly in adults. It is ordinarily located at a pole of the kidney (more often the lower), is a solitary tumor developing to great size, and usually is very vascular. Different portions show great variation in appearance, soft and yellow where the clear cells predominate, dark where there has been hemorrhage, and divided into lobules of varying size by strands of fibrous stroma. There may be cysts or calcification secondary to necrosis of tumor cells. The tumor tends to extend into the pelvis of the kidney and invade the renal vein. It may grow slowly and is often overlooked until evidence of metastasis is found. The lungs and bones are the

most common sites of metastasis and as much variation in the histology of the metastatic lesions may occur as in the primary tumor.

Whitmore stated that the most confusing cases were the hypernephroid tumors in which metastases show changes partly hypernephroid and partly sarcomatoid. These findings were explained on the basis of the law of "genetic restriction." As development advanced, a constantly increasing restriction in the differentiation of tissue occurred. The tissue or organ was more rigidly bound to its particular type of differentiation than was the generalized material from which it originally came. In neoplasia, tissues conform to this law, that cells do not necessarily lose their



Fig 2 Papillary adenocarcinoma of kidney a Metastasis to the lung b, Lateral displacement of the pelvis with marked angulation of the upper portion of the ureter

c This photograph of specimen shows involvement of the entire kidney with an abscess cavity in the tumor

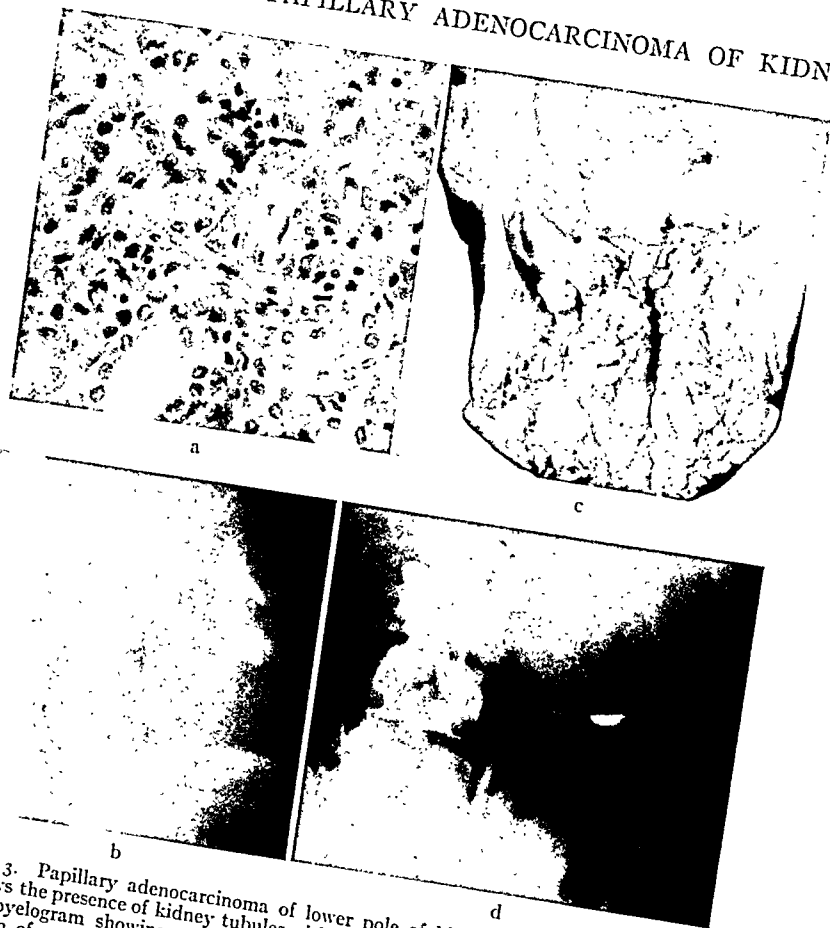


Fig. 3. Papillary adenocarcinoma of lower pole of kidney in an elderly female. a, Shows the presence of kidney tubules with lack of cellular differentiation. b, Retrograde pyelogram showing marked retraction of calyces downward with abnormal insertion of ureter. c, Hypernephroid mass involving the lower third of the kidney. d, Retrograde pyelogram of a gigantic hydronephrosis erroneously diagnosed as a renal tumor and erroneously treated by roentgen-rays. Nephrectomy with recovery.

potentiality to differentiate in more than one direction. One potentiality may become pre-dominant, another recessive.

We will forego further discussion of the pathological varieties of tumor of the kidney and pass on to practical consideration of the diagnosis and treatment.

#### DIAGNOSIS

The fact that kidney tumors are difficult to detect early accounts for the high mortality. Recent refinements in urologic diagnosis make it possible to detect the presence of these tumors at an earlier stage and thus reduce the high mortality caused by delay in diagnosing them correctly.

The symptoms of pain, 35 per cent, blood in the urine, 50 per cent, and mass in the flank, 10 per cent, are rarely concomitant, but when present make the diagnosis obvious. We must continue to impress upon the laity the fact that a passage of blood from the urinary tract is evidence of grave import, and that such a sufferer be examined at once. The amount of blood may be slight or profuse and the only finding for a long period of time. Blood clots may block the ureter and cause colic-like pain on the affected side. The fact that bleeding may be painless, intermittent, and of short duration lulls the patient into a false sense of security. An important finding is loss of weight and strength, 15 per cent. The pres-



Fig 4 Enormous cystic tumor involving the entire kidney a, Section of tumor showing moderate cellular differentiation with some mitotic figures present b, Retrograde pyelogram showing marked elongation and retraction

with partial amputation of the minor calyces. Downward displacement of the pelvis is also present in this case c, A large calcified cyst is noted. The mass measured 12 by 24 centimeters

ence of a large mass in the loin is usually a late manifestation of tumor of the kidney and indicates a poor prognosis.

Metastases (blood borne) may cause gastrointestinal distress, headache, cough, shortness of breath, constipation, and jaundice. Fever, leucocytosis, hypertension, and varicocele on affected side are frequently observed. Renal tumors become very large, tender on pressure, do not move with respiration, and are usually found in patients of from 50 to 70 years of age. Sixty to 70 per cent occur in males, and a majority die within 2 years from cachexia or metastasis.

The study of such a case would include a preliminary intravenous urogram to deter-

mine the comparative size, function, and appearance of the calyces and pelvis of the kidney. A cystoscopic examination should then be made, including bilateral retrograde pyelograms and a differential function test. Evidence of retraction, blunting, amputation or absence of a major calyx is the most characteristic pyelographic finding and is present in a majority of cases. The number of calyces involved increases with the size of the tumor, usually but one major calyx being primarily affected. Elongation by extension of the tumor toward the periphery may give the calyx deformity a "spiderleg" appearance.

The absence of deformity of a calyx or of the pelvis may be misleading, as we have seen 2

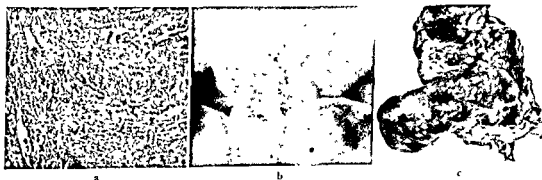


Fig 5 Papillary adenocarcinoma of the left kidney in an elderly male a, Section of the tumor showing well marked lumen and the typical papillary structure with little cellular differentiation b, Retrograde pyelogram of the

left kidney showing marked elongation of the minor calyces c, The large mass involving the lower pole of the kidney. Prostatic hyperplasia, producing acute retention, was also present

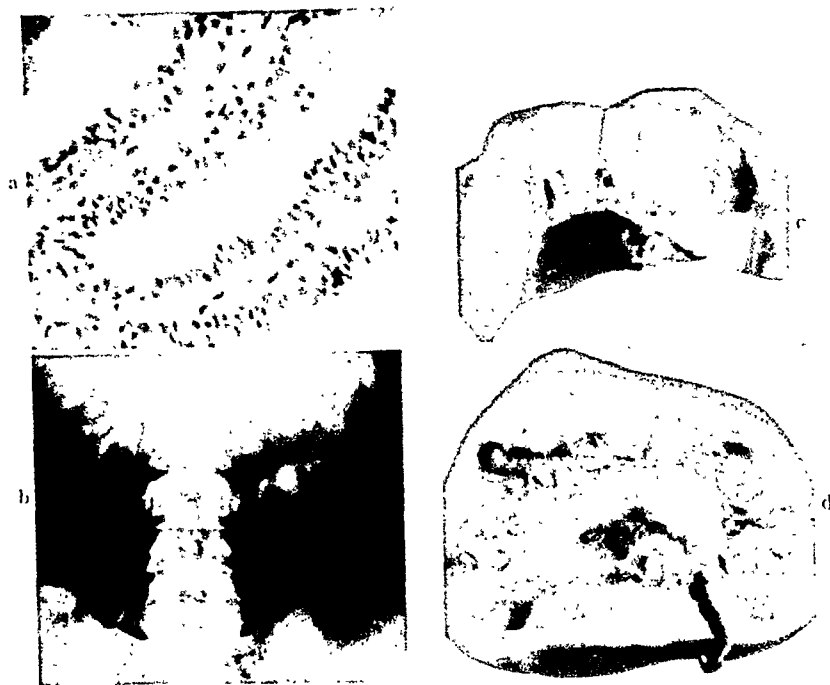


Fig. 6. Malignant papillary cystadenoma of kidney with fungating growth in pelvis. This tumor arose from simple cystadenoma, and represents a subdivision of papillary adenocarcinoma. a, Papillary structure within cystic cavity. b, An intravenous pyelogram. c, Tumor involving the pelvis and cortex seen invading but not extending beyond the renal capsule. d, Fungating growth in pelvis.

cases in which the calyces and pelvic outline were normal in the retrograde pyelogram, only to find evidence of deformity on intravenous study. Too much reliance, therefore, should not be placed on the findings in a single pyelogram.

Other evidence of deformity includes compression of the pelvis of the kidney, producing flattening, narrowing, or obliteration. Filling defects may be noted, as a result of the presence of blood clots or a tumor. The kidney may be displaced laterally, superiorly, or medially, with abnormal insertion of the ureter. The latter is a very significant finding. Deformity of the ureteropelvic junction or alteration in the silhouette of the kidney is frequently observed.

The differential diagnosis includes pyonephrosis or hydronephrosis, solitary or polycystic kidney and infections producing hematuria and pyelitis cystica or glandularis. Two cases of this type were recently observed.

Ptosis, rotation, or the presence of a double kidney may be mistaken for tumor. We have had 5 cases in which prostatic hypertrophy was found in association with tumor of the kidney. Even in a case of prostatism the possibility of a tumor of the kidney should be considered if there is a passage of blood.

On cystoscopic examination, hydronephrosis of the closed type may be difficult to differentiate from tumor, especially when an obstruction is found in the upper ureter. This occurred in 2 of our cases, 1 of which had received roentgen-ray treatments elsewhere for a mass erroneously thought to be a neoplasm. The patient had been assured that this treatment had reduced the size of the mass despite the fact that it contained only urine.

A retroperitoneal tumor (non-renal) may cause marked displacement of the kidney, so the degree of renal mobility should always be determined. There is less retraction of the calyces in polycystic kidney than in



Fig 7 a, High power section from an adrenal rest tumor, showing sheaths of large polyhedral cells with vesicular nuclei and clear cytoplasm. In many areas the tumor cells are spindle shaped. Other sections show the characteristic papillary adenocarcinoma with well marked lumina. This is an unusual type of tumor (Ewing). b, Whole kidney section with involvement of the lower pole by the tumor described (Whitmore technique).

tumor, and it is usually bilateral. When retraction does occur, however, it is broad, in contrast to the narrow calyces found in neoplasm. The pyelogram in solitary cyst is often unaltered and the urine normal. In one instance, we found the position and axis of the kidney to be considerably altered by the weight of the cyst.

An exploratory operation, implying a possible nephrotomy, is never indicated in tumor of the kidney, particularly if the patient has been subjected to preliminary roentgen-ray therapy. Certain of these tumors are so radio-sensitive that marked shrinkage will occur following irradiation, thereby distorting the pyelogram and give erroneous conclusions.

Occasionally one sees a case in which evidence of deformity is found on intravenous pyelography, only later to have this proved erroneous by a retrograde pyelogram. This finding has occurred in our experience. In such instances it is important to repeat the retrograde pyelogram at regular intervals

until one can rule out the possibility of a tumor. Aspiration biopsy should be practiced in doubtful cases, particularly in suspected cystic disease.

#### TREATMENT

The feasibility of operation in kidney tumors should always be carefully weighed. With a history of short duration and the presence of a fixed mass producing toxemia, the advisability of operation is questionable, as the tumor is obviously highly malignant. In such instances, one may proceed with a course of roentgen-ray therapy, and if marked diminution in the size of the tumor occurs, it may be removed 6 weeks later. This delay allows sufficient time for fibrosis of the vessels to take place and also permits the skin to regain some of its vitality.

The question of metastases should always be determined prior to operation, preliminary roentgenograms being made of the lungs, lumbar spine, pelvis, long bones, and skull.

Metastases are more frequent in highly malignant tumors. In some instances, extirpation of the renal tumor and metastatic process has been practiced, the inference being that removal of the renal tumor will slow down the tendency toward further metastasis.

Calcification within the tumor is evidence of necrosis and has little bearing on the degree of malignancy.

The avenue of surgical approach should always be carefully considered in the presence of a large renal mass. The transperitoneal approach offers the best method of obtaining early and adequate exposure of the pedicle and exploration of the renal vein. The mass can then be removed with less trauma, thus obviating the possibility of tumor tissue being squeezed into the renal vein. We remove large tumors by this route and find it very satisfactory. If the tumor is small, involves the pelvis of the kidney, or the diagnosis is uncertain, the lumbar route is preferable. Resection of one or more ribs facilitates removal of a large tumor, and should be practiced if the lumbar approach is used.

Roentgen rays may reduce the size of the tumor, and in certain instances it will shrink as much as 40 per cent, thus facilitating re-

moval. This modality does not make an inoperable tumor operable, but in radiosensitive ones it does produce shrinkage. Postoperative radiation in most cases is without value if removal has been clean. Dean stated that recurrence of the tumor cannot be prevented, but that occasionally local recurrences of the tumor in the incision may be inhibited. Nesbit stated that routine preliminary irradiation of a tumor is not practiced in his clinic.

Hand and Broders found definite clinicopathological correlation between the grade of malignancy, operability and expectancy of life after operation.

The fact that one-half of the patients die within 2 years after removal of renal tumors makes the advisability of an operation questionable in patients with large fixed tumors of short duration, in which the general condition of the patient is below par.

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## THE ACUTE GALL BLADDER

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**D**URING the last 10 years, the debate on conservative versus surgical management of acute cholecystitis has continued with probably more evidence being produced in favor of serious surgical consideration in every case. It has been only within the last 4 years that my personal ideas have come to agree with this latter viewpoint. I can truthfully say that this change has come about through some rather unhappy observations and experiences as well as through a close study of reported series of cases.

This article deals with an analysis and breakdown of 44 cases in which the clinical diagnosis of acute cholecystitis had been made. The cases are divided into two groups. The first group of 22 consecutive cases represents a period in which my policy was not to operate for acute cholecystitis unless certain signs, symptoms, or laboratory findings were reasonably definite, although in several instances the decision to operate was based entirely on that inexact factor of practical medical science called "clinical impression." The second group is comprised of an equal number of cases of acute cholecystitis seen during a later period in which my policy has been to operate more readily unless there is definite early abatement of signs, symptoms, and laboratory findings, with definite improvement in the patient's general appearance and no evidence of that "stationary loginess and apathy" which is often seen in patients with progressive pathological changes of gangrene, abscess, or perforation but whose temperature, pulse, and blood picture approach normal. The lack of parallelism between the pathology and the laboratory-clinical findings is often more astounding in acute cholecystitis than in acute appendicitis, and the clinician's insecurity when attempting to evaluate these patients will be discussed later. It may be said that

the first 22 cases were handled under the policy of probable nonoperative treatment with surgery done in only 8 cases, or 36.4 per cent, and the second group under the policy of probable operative treatment, with surgery done in 16, or 72.8 per cent, of the 22 cases. It must also be taken into consideration that this is a breakdown of 44 patients, most of whom had already been hospitalized.

To illustrate further the lack of parallelism between laboratory-clinical findings and the degree of pathological change in cholecystitis, one has only to mention a pathogenesis encountered by every surgeon who performs cholecystectomies, and that is finding an advanced acute gall bladder disease in which the diagnosis of chronic gall bladder disease has been made. Thus, the lack of parallelism can rightfully be emphasized whether we look at the disease from the chronic or the acute phase. Fallis and McClure stated that 10.9 per cent of their 320 cases of acute cholecystitis had been diagnosed as chronic cholecystitis. Wesson and Montgomery reported an incidence of 28.9 per cent in a series of 76 cases of acute cholecystitis. The author's series does not include any cases in which the diagnosis of chronic cholecystitis was made and an acute cholecystitis found at operation, but this is experienced not too infrequently.

Admitting the lack of parallelism, we must then consider the frequency with which the acutely inflamed gall bladder does undergo gangrene, abscess, or perforation with or without analogous variations in temperature, blood, or clinical findings, in order to determine whether these advanced pathological changes occur often enough that we dare not disregard this factor. The majority of authors reporting on this incidence have been forced to place the figure between 10 and 30 per cent. Berk, in an analysis of 8,752 cases reported by many authors, reveals that 1,540, or 17.9 per cent, of these cases progressed to gangrene, abscess, or perforation. Fallis and McClure report that gangrene and perforation occurred

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## BEST: THE ACUTE GALL BLADDER

TABLE I.—ANALYSIS OF 44 CASES OF ACUTE CHOLECYSTITIS

	Nonoperative No.	Operative Per cent	Operative No.	Operative Per cent
Patients not operated upon.....	14	63.6	6	27.2
Patients operated upon.....	8	36.4	16	72.8
	22		22	
Patients treated.....	3	13.6	1	4.5
Mortality Group.....	3	37.5	1	6.2
Operative.....				

in 15.9 per cent of their series of 320 cases. Taylor placed the figure at 22.5 per cent of 129 cases and Touroff at 20 per cent of 75 cases. Clute and Lembright reported an incidence of 14 per cent in 29 cases, and Heuer 26 per cent in 153 cases. In considering the mortality for this same group, one finds Fallis and McClure quoting 9.5 per cent, while the mortality for their entire series was about one-half of this figure, or 5.3 per cent. In other words, even though surgery is indicated, and the patients are under the care of surgeons who favor early surgery in this group. It there is a high mortality to know just how high would be interesting to know just how high the mortality for the 320 cases would have been if they had been controlled by one favoring conservative treatment rather than operative intervention. No doubt a considerable number were prevented from progressing to gangrene, abscess, or perforation by early operation.

The element of time between onset of illness and time of operation is an important factor to be considered. Taylor reported a mortality of 16.3 per cent for his 129 cases of acute cholecystitis, but analysis shows that for those patients operated upon before the fifth day, the mortality was only 5 per cent, while for those operated upon after the fifth day it was 23.8 per cent. Further analysis shows that the greater percentage of the purulent and gangrenous cases were among those patients operated upon after the fifth day. Clute and Lembright had only 1 death in 29 patients, a mortality of 3.4 per cent, and this was a late case of perforation. Heuer reported a mortality of 3.2 per cent for his 153 cases, but for the 16 patients with perforation the mortality was 12.6 per cent.

It is a rare occasion, however, when immediate or emergency operation is indicated. In most cases, some hours to several days should be given to observation and adequate preparation of the patient for operation, depending somewhat on the assumed pathological picture, or a higher mortality rate will be the inevitable result.

Cave, in discussing the surgical treatment of acute cholecystitis, used the term "immediate" for the first 24 hours, "early" for 48

hours to 7 days, and "delayed" for those cases in which operation was postponed until complete remission had taken place. This seems to be an excellent and practical classification. Fallis and McClure, in their analysis of 320 cases, made the following division: immediate operation—first 24 hours—with a mortality of 8.4 per cent; early operation—24 to 72 hours—with a mortality of 7.3 per cent; and delayed operation—after 72 hours—with a mortality of 3.4 per cent. However, they always followed the practice of operation for acute cholecystitis. Taylor arrives at his mortality figures by grouping his 102 patients into those operated upon within 48 hours of acute onset, those between 2 and 5 days, and those after 5 days, the mortality for the first group being 5.2 per cent, for the second 5 per cent, and for the third 23.8 per cent. This latter high figure dramatically reveals the danger of delaying operation too long. Zininger, with a similar classification for time of operation, shows an increase in the mortality rate from 6.6 per cent for those in the 2 to 5 day period, to 25 per cent for those after the 5 day period. Carter, Greene, and Twiss, in an analysis of 514 cases of acute cholecystitis, also emphasize the "time element after onset." For 81 patients operated upon within 24 hours of onset, they had a mortality rate of 15.1 per cent; for 137 patients operated upon between 2 and 4 days after onset, 5.9 per cent; and for 192 patients, between 4 and 7 days, 7.7 per cent; and for 192 patients, between 7 and 50 days a mortality of 16.7 per cent. Considering the entire group, the optimum time for operation seems to be somewhere between 2 and 7 days, and in view of individual patient variations, this figure of 2 to 7 days is not too wide. My own analysis of some of the cases reported in the literature

TABLE II.—AGE INCIDENCE AND OPERATIVE MORTALITY IN ACUTE CHOLECYSTITIS

Author	Yrs of age	No patients	No deaths	Per cent mortality
Fallis and McClure	30 to 40	108	1	0.9
	40 to 60	164	11	6.7
	60 plus	48	5	10.5
Best	46 to 50	2	0	0
	50 to 60	24	1	4.1
	60 plus	18	3	16.6

and of my personal experiences would seem to favor the "early operation" classification, placing the optimum time to operate somewhere between the second and seventh day, depending upon the individual case. This allows time to build up local and general resistance and immunity, most cases will not have progressed into the most dangerous stage, the patient will not have used up his reserve, and liver damage will not be too great. Cave believes that postoperative deaths are more often the result of liver damage than anything else. From the figures given, it can be interpreted that, if subsidence does not begin promptly and uninterruptedly, there is great danger of gangrene, abscess, and perforation taking place, and the mortality rate will be higher with or without operation as the patient goes by the 7 day period.

In my own series, among the first group of 22 patients in which the general policy was to avoid operation except as untowardly indicated, 8, or 36.4 per cent, proved at operation to have gangrene, abscess, or perforation. These were all individuals over 48 years of age, 6 of them being between 55 and 76 years of age, with an average age of 62 years. Three deaths occurred resulting in an operative mortality of 37.5 per cent, and a mortality for the entire group of 13.6 per cent. Two of the patients who died were 64 and 72 years of age, respectively. Cholecystostomy was performed 3 times with 2 deaths and cholecystectomy 5 times with 1 death. All of these patients were operated upon 5 days or more after the acute onset, and some as late as the twentieth day. It has been said that pathologists see very few cases of perforation at the autopsy table. The answer to that is that hospitals with pathologists usually have capable surgeons who operate when certain signs or symptoms

appear or when there is too much uncertainty, and if death ensues the case goes to the post-mortem room as an operative death for acute cholecystitis, while in the institutions that do not employ pathologists, autopsies are the exception and no records are available as to what occurs in the particular acute abdomen. Personally, I have seen 2 unoperated, ruptured gall bladders at the autopsy table, one in a patient of my own who refused operation. In the 8 operative cases of this group, the parallelism between the clinical picture and pathological findings was definitely lacking in 4 patients, 2 of whom died.

In the second group of 22 patients, seen during a period when I favored probable operative treatment as heretofore discussed, 16, or 72.8 per cent, were operated upon within 7 days and 6, or 27.2 per cent, fully recovered from the attack of clinical acute cholecystitis without operation. Three, or 13.6 per cent, of those operated upon had marked pathological changes in the gall bladder but no generalized peritonitis because of the protective matting of the greater omentum. This is a marked improvement over the percentage in the first group. Three of the remaining patients had areas suggesting early gangrene, and 2 had acutely inflamed gall bladders with pus in the common duct. In the 16 patients operated upon, the common duct was opened 4 times—25 per cent—stones being found in 3 of these, or 18.7 per cent. Cholecystostomy was done 5 times and cholecystectomy 11 times. All 3 patients with gangrene, abscess, and perforation were over 50 years of age, 2 of them past 60, the average age being 63 years. One death occurred in this group, which gives a mortality of 4.5 per cent for the entire group as compared with 13.6 per cent in the first group, and an operative mortality of 6.2 per cent as compared with 37.5 per cent in the first group. The patient who died after cholecystectomy was 68 years of age, and was not operated upon until the seventh day, at which time a gangrenous gall bladder was found. She was a rather obese woman, with a thick abdominal wall. Her temperature did not rise above 101 degrees, her pulse was 76 to 86, the highest white cell count was 11,000 and this came down to 6,000 on the fourth day. The staff

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count varied between 10 and 15 per cent. After the third day, the patient had very little tenderness but she did have a "stationary loginess and apathy" and possibly operation on the fourth or fifth day would have prevented this exodus. Of the 6 not operated upon, 2 have since received surgical treatment, one for recurrence of acute cholecystitis and stones in the common duct, the other because of recurrent acute cholecystitis associated with jaundice and pancreatitis. Both have recovered from their operations.

Since an analysis of all available data reveals that operation for acute disease of the gall bladder after the first or second day does not initiate greater spread of infection or harm to the patient than does operation for ordinary acute appendicitis, and that in both instances mortality occurs in that group which progresses into gangrene, abscess, or perforation, there is considerable evidence and argument that clinicians should not permit cholecystitis to reach such an advanced stage. However, one cannot compare the pathological process of the gall bladder with that of the appendix, in all respects, for cholecystitis usually is caused by a vascular disturbance and most appendices have an inciting infective factor. Studies on the relationship of bacteria to acute cholecystitis by Denton, Wilkie, Branch, and Andrews, as well as some others, have produced rather convincing evidence that infection is not the primary etiological factor. In 1933, Andrews reported from quantitative bacteria studies that no more bacteria were found in acute gall bladders than in quiescent ones. This was true of his studies on empyema and gangrene of the gall bladder also. The authors mentioned as well as others conclude that mechanical and circulatory factors account for the majority of gall-bladder lesions. One should also include the hepatometabolic disturbance resulting in crystallization of cholesterol or the precipitation phenomena which in turn causes trauma of the cystic duct with secondary edema, inflammatory reaction, and subsequent interference with the blood supply. Clute ably compares the early acute gall bladder to an ovarian cyst with a twisted pedicle from the angle of signs, symptoms, laboratory findings, and the postoperative

course. Of course, in the later stages the chemical disturbance associated with bile and its closer connection with the lumen of the gastrointestinal tract would tend to make an acute gall bladder a more critical problem, even though the undiagnosed and unoperated upon ovarian cyst with a twisted pedicle is a serious event.

After recognizing the danger accompanying gangrene, abscess, and perforation and admitting the lack of parallelism previously mentioned, we must search for any minor details which may help in earlier recognition of the need for surgery. From my own experience, no symptom, sign, or laboratory finding is infallible, and of late it has been my practice to advise surgery if any one of these is the least suggestive that all is not well. It is hardly necessary to mention here that a septic course revealed by signs, symptoms, or laboratory findings indicates surgery. It must be emphasized, however, that a temperature which does not subside even though pulse, white cell count, and physical findings are normal must be viewed with great alarm, as should an increased pulse rate with normal temperature, white count, and physical findings, or continued pain, tenderness, or rigidity with normal temperature, pulse, and white count. Surgery is probably indicated in all such cases. If the white count remains high, it certainly indicates that complete and safe subsidence has not occurred. In my own experience, too frequently the white cell count has dropped to normal or even subnormal, and later operation has revealed gangrene, abscess, or perforation. However, in most cases in which the white cell count has been misleading as well as the other laboratory-clinical findings, I have found that a careful analysis of the differential white count (Schilling) reveals either a definite swing to the left with increase of the younger forms of white cells or an increase in the staff forms to over 10 per cent. I do not believe that too much emphasis can be placed on this observation. It has been my inclination in many instances when dealing with an acute abdominal lesion in which the white count remains within normal, or even subnormal, limits to gauge the actual white cell count in terms of degree of infection by

placing three zeros after the number of staff forms and to consider that as the actual number of white blood cells. Thus, a total white cell count of 6000 with a staff count of 12 per cent would be considered a 12,000 leucocyte count. I feel this has frequently led me to operate in acute abdominal lesions when other findings were of no value in judging for or against operation. Of course, as stated before, this method is not infallible. Another factor which I believe is particularly helpful in evaluating the status of acute cholecystitis or its complications has been the "stationary loginess and apathy" which is usually manifested in those patients in whom other findings are not indicative of an advanced pathological state. A remaining shadow of the gall bladder or right upper quadrant haziness on a flat plate x-ray should also make one suspicious that all is not in order in the right upper quadrant even if all other signs, symptoms, and laboratory findings are within normal limits.

That age apparently plays a definite rôle in the mortality has previously been brought to our attention by Judd and by Heuer. In people over 50 years of age and especially those over 60 years of age, the tissues have less elasticity, and with the distention associated with cystic duct obstruction there is earlier and greater interference with the blood supply to the gall bladder. Then because the elasticity of the gall-bladder wall is also diminished, pressure gangrene or perforation with localized abscess or generalized peritonitis is very likely to occur quite early. It is in these elderly patients that the surgeon would like to delay operation, but analysis of most mortality tables reveals a much higher mortality for this group because of the greater incidence of gangrene, abscess, and perforation, and therefore this group actually needs serious surgical consideration.

Although cholecystectomy is the operation of choice in acute cholecystitis, it should not always be the operation of selection. Some authors are able to report a very high percentage of cholecystectomies but my own personal experience gives only 66.2 per cent cholecystectomies and 33.1 per cent cholecystostomies in the 24 patients operated upon.

During the last several years, in cases of acute cholecystitis, I have been performing cholecystectomies more frequently by using the method of Thorek. The gall bladder is emptied with a trocar and suction after the operative field has been well packed off, and then is excised from the fundus down to the cystic duct on either side close to where it meets the liver surface. This portion of the gall bladder is removed and the mucosa remaining on the liver surface is then coagulated or cauterized with the electrocoagulating current or with phenol and alcohol. The cystic duct is ligated or drained with a catheter, and a running catgut suture is closed over the remaining gall-bladder mucosa on the liver surface. In my own patients, I insert a soft rubber drain (Penrose) down over the sutured gall-bladder bed to the cystic duct and right kidney area, bringing the drain out through a separate stab wound incision. Of course, in some cases the routine cholecystectomy technique may be used without additional difficulties.

The common duct may be opened directly for complete exploration of the duct, which I believe is the better method, or less preferably the cystic duct may be split down to its junction with the common duct. In neither acute nor chronic biliary conditions have I found it very satisfactory to explore the common duct through the cystic duct as the cystic ducts which I have encountered have usually been too small. If the common duct wall has been opened a T-tube is inserted. The arms of the T-tube should be shortened and bevelled, and a small piece of rubber should be removed from the transverse portion opposite the attachment of the long arm. If the common duct has been explored through the cystic duct, a catheter should be slipped through the cystic duct into the common duct. The common duct was opened in 6 or 25 per cent, of the 24 patients operated upon in my series and stones were found in 4 of these, or 16.6 per cent. In 1 of the 2 other cases, the delayed cholangiogram revealed a hepatic duct stone which could not be removed by the biliary flush because of its size. This patient succumbed at a secondary operation 3 months later. Choledochostomy was indicated in

several other cases because of the history of jaundice, but the condition of the patient or other difficulties did not warrant it at the time of operation. An argument against operation for acute cholecystitis is the ever present edema and advanced inflammation in the region of the common duct which makes its identification difficult. This is a logical argument when one is "common duct stone conscious," for about 90 per cent of all acute cholecystitis cases have stones within the gall bladder and probably 20 per cent of these will have stones in the common duct also. However, we sometimes have to choose the lesser of two evils. My faith in the biliary flush leads me to believe that it will probably answer the question in many of these cases retaining smaller common duct stones if it is used routinely following surgery.

If cholecystostomy is selected because of the general condition of the patient or because of fear of spreading toxic or infective elements, a large tube close to  $\frac{1}{2}$  inch in diameter, preferably with a flange such as a mushroom catheter with part of the base removed, is placed in the gall bladder. The smaller stones may pass out through the tube, and if necessary later, the gall bladder may be explored with the cystoscope as suggested by Hollenberg and Eikner. Little can be deduced from the mortality figures of cholecystostomy versus cholecystectomy, for the patient on whom cholecystostomy is done is usually more acutely ill and a poorer operative risk and naturally a higher death rate ensues.

On several occasions when the patient was moderately jaundiced at the time of operation but the common duct was not opened because of marked local edema and inflammation or because the patient's general condition was rather poor and no stone was grossly palpable, a thickened elongated cystic duct with or without stone was found bound down and angulated into the common duct in such a manner as to cause pressure on the common duct with probable partial obstruction. The cystic vessels seem to take part in this mechanism by acting as a bowstring holding the enlarged, thickened gall-bladder neck and cystic duct in a crowded position against the common duct. This probably is a definite

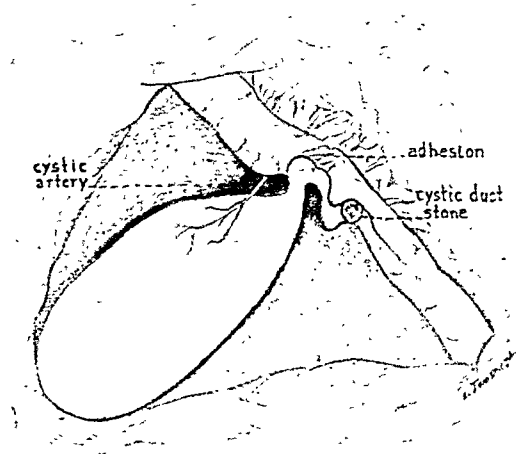


Fig. 1. The cystic vessels may act as a bowstring in acute cholecystitis and the enlarging, edematous cystic duct, with or without stone, become compressed against the common duct, causing partial to complete obstruction of the common duct.

entity and, although it explains some cases of jaundice, it does not definitely rule out common duct stone (Fig. 1).

In those cases in which the common duct has been opened and a T-tube or catheter inserted, it is most important that a delayed cholangiogram be made sometime around the seventh to tenth day, as one cannot search as diligently for stones in the common duct in the acute case as in the chronic case, and experience with cholangiography in chronic cases reveals the occasional finding of a remaining common duct stone. If a stone is portrayed, an attempt should be made to dislodge it with the routine 3 day biliary flush regimen and ductal irrigations as previously described.

If the stone is lodged above the T-tube in the hepatic duct, the T-tube should be removed so the stone can travel down to the lower end of the common duct. If the stone is too large to pass through the sphincter area an attempt should be made to break it up by instilling 5 cubic centimeters of a mixture of  $\frac{2}{3}$  ethyl ether and  $\frac{1}{3}$  ethyl alcohol into the common duct by the modified method of Pribham. Then if the cholangiogram reveals a disrupted stone, the flush should be repeated a number of times. In any event, after a tube or catheter has been removed, the patient

should be given the flush to wash out remaining debris

A delayed cholangiogram should also be made in every case of cholecystostomy as it may give considerable information. For instance if the cholangiogram reveals a blocked cystic duct, the indwelling catheter should not be removed because, as the skin closes over, it leaves a blind mucosal pouch and one can anticipate a recurrence of the condition. If the cystic duct is blocked by edema rather than stone, hot packs together with warm saline and olive oil irrigations may cause the duct to become patent again. This can be ascertained by repeating the cholangiogram. If the cystic duct is blocked by a stone or if a stone is found in the gall bladder, an attempt may be made to break up the stone with the ether-alcohol mixture. Although I have never had particular success with this method there have been some encouraging reports on it. Another method for removing stone or stones remaining in the gall bladder is by means of the cystoscope, as described by Hollenberg and Eikner. Stones remaining in the gall bladder or a blocked cystic duct are indications for cholecystectomy.

Finally it must be stated that although a patent cystic duct with no stones remaining in the gall bladder favors no further recurrence of the gall bladder symptoms, we know that this is not assured and every patient who has a cholecystostomy for acute cholecystitis is a potential candidate for later cholecystectomy.

#### SUMMARY AND CONCLUSIONS

1. The incidence of gangrene, abscess, and perforation in acute cholecystitis is between 10 and 30 per cent, and as in appendicitis the mortalities are mostly in this group. By approaching the case with a surgical attitude and deferring operation only when there is no confusion of signs, symptoms, laboratory findings, and appearance of the patient, the mortality for acute cholecystitis may be reduced.

2. The incidence of gangrene, abscess, and perforation is higher in the older age group, beginning with 50 years and especially after 60, and this group of cases carries the higher mortality rate. One should approach this group with a more definite surgical attitude.

3. In group 2 of my own series, in which all patients were approached with a definite surgical attitude, 72.8 per cent were operated upon early and only 13.6 per cent of the patients had advanced gangrene, abscess, or perforation. Only 1 death occurred in this group. In retrospect, in some of the patients operated upon the conditions might have subsided after 1 or 2 more days of observation. Probably about 50 per cent of cases of acute cholecystitis in any series should come to operation to give the lowest mortality for acute cholecystitis, but again it must be emphasized that any confusion of signs, symptoms, laboratory findings, including the haziness of the right upper quadrant in the flat x-ray plate, indicates a need for operation.

4. If the differential count reveals staff forms above 10 per cent, one should be suspicious of a nonsubsiding acute cholecystitis. In this group of cases, this was a fairly constant finding but not infallible.

5. As to appearance, a "stationary loginess or apathy," particularly in the older group, seemed to be a characteristic of nonsubsiding acute cholecystitis.

6. About 90 per cent of patients with acute cholecystitis have associated gall stones and about 20 per cent of these will have stones in the common duct. If the acute inflammatory reaction will subside, there is later a better opportunity to explore the common duct.

7. Probably it is safer to favor early operation and operate only upon about 50 per cent of the patients than to favor conservative treatment and operate only after advanced complications have arisen. In 2 groups of 22 patients each, the group mortality was reduced from 13.6 to 4.5 per cent by favoring early operation in about 70 per cent of the second group.

8. Delayed cholangiography when possible and the routine biliary flush are most important in the management of these cases.

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## HOW TO USE CATGUT

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THERE is one very real reason for writing on the use of catgut; namely, because the subject is so seldom dealt with in the literature except in a very fragmentary manner in textbooks. During the past 5 years, there has only been one article published on how to employ catgut to the best advantage, although there have been many articles on how to use silk. Catgut is the most widely used suture material, and the paucity of published comments undoubtedly accounts for its widespread poor usage and the confused ideas about this usage. Tradition still governs the employment of catgut, while knowledge regarding the process of wound healing has steadily advanced. In this paper, suggestions are made for improving the use of catgut based on the physiology of wound healing.

### THE SELECTION OF CHROMIC OR PLAIN CATGUT

Whether to use plain or chromic catgut can be decided only on the basis of the healing properties of tissues in which the sutures are to be employed. Chromic catgut is absorbed more slowly than plain and keeps its thread strength longer. Plain catgut, therefore, is used when rapid healing is to be expected, as occurs in serosa and mucosa covered surfaces, and for ligatures, because the blood clots quickly. For the very large arteries, however, chromic catgut must be used, for the proliferation of fibrous tissue is the only insurance against postoperative hemorrhage. Plain cat-

gut is also indicated when the object of the suturing is only the obliteration of dead space to prevent "laking" of serum or blood. Dead space is found most frequently in muscle and fat.

Chromic catgut is used to suture those tissues which give immediate strength to the wound and which will maintain a sufficient amount of this strength to prevent separation of the cut edges until the time when the wound develops its own strength through the process of healing. Fortunately, those tissues which have the most holding power for sutures likewise develop the most strength during the healing of the wound. These are the fasciae, connective tissues of all descriptions, and the muscularis mucosae in the wall of the gastrointestinal tract.

### THE TISSUES WHICH TOLERATE CATGUT POORLY

Catgut should be used sparingly or not at all in those tissues which tolerate catgut poorly. The tissues which tolerate catgut poorly are: (1) the skin, (2) the subcutaneous fat, (3) mucous membranes, and (4) the muscles. The degree of toleration varies for each of these tissues and for different reasons.

The skin always harbors bacteria in the hair follicles regardless of the character and the amount of antiseptic used to cleanse its surface. Three or four days after catgut is inserted in the skin, these bacteria begin to grow around it. Inflammatory changes follow, and the strand is rapidly destroyed regardless of



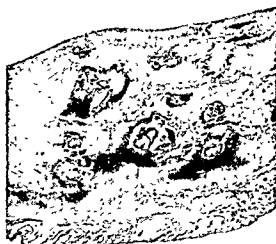


Fig 1 Eight pieces of catgut in small area of tissue (After Vivier)

the size or degree of chromicization. Because of the tendency toward pus formation and premature absorption, catgut absolutely should not pierce the skin, although it may be used successfully as a subcuticular suture.

In the subcutaneous fat, the absorption of catgut, or more specifically the chemical and cellular reaction which brings about this absorption, tends to cause some necrosis, induration, and the elaboration of a small amount of serous exudate. The most common cause of induration of the wound sutured with catgut and of the escape of a small quantity of serous fluid on the tenth to the twelfth day of healing is the presence of too much catgut in the subcutaneous fat. Sutures in the subcutaneous fat contribute no strength to the wound anyway. If this layer is thick dead space will inevitably form, but obliteration of it can be accomplished in other ways which will not produce induration. The subcutaneous fascia may be sutured with very fine, small bite, interrupted sutures of plain catgut, No 0000 or No 000000, or tension sutures may be used. The fascia in the subcutaneous fat, even when invisible, can be easily located by means of rat-toothed forceps. These forceps pull out of the fat while they hold in the fascia.

Although wounds in mucous membranes heal rapidly, the earliest possible restoration of the continuity of their cut edges is desirable

As in the skin, this approximation creates an effective barrier against further bacterial contamination. However, mucous membranes slough where pierced by sutures unless they are extremely fine. Bower has shown that No 00000 catgut is well adapted for suturing mucous membranes, yielding rapid primary healing with minimal tissue reaction. Unabsorbable sutures also slough from mucous membranes unless they are extremely fine. If they do not, permanent ulcerations are apt to remain about them where they penetrate the surface. Calculi form around unabsorbable strands extending through the mucous membrane of the gall bladder and urinary bladder.

Muscle tolerates catgut better than fat, but also tends to necrose and bleed easily—a tendency likewise exhibited toward unabsorbable sutures. Muscle possesses so little holding power for sutures anyway that the mechanical advantage gained hardly justifies the trauma of inserting them. Because of the lack of holding power, sutures frequently pull out of muscle within the first 4 days of healing. On the other hand, the sheaths of muscle should always be sutured, for they do possess holding power for sutures and do not necrose easily. When a large muscle bundle is cut across, interseptal fasciae should be sutured individually. For collapsing dead space in muscle, fine sizes, No 000, of plain catgut will give the best result.

#### HOW MUCH CATGUT SHOULD BE USED IN CLOSING A WOUND?

The best answer to the question of how much catgut should be used is, "Less than is generally thought to be required." Many of the untoward reactions exhibited by healing wounds sutured with catgut, the so called allergic and tissue hunger reactions, are really foreign body reactions caused by the use of excessive amounts of catgut. Catgut is used in such large sizes and in such large quantities that the tissues are simply overwhelmed. Edema and leucocytic invasion naturally occur, and the tissues thicken and become indurated. These changes can be seen in Figure 1, reproduced after Vivier. There are 8 pieces of catgut in a small area of tissue, and indeed the cross sections of catgut are more apparent than the areas of tissue between

In the suture of wounds, catgut is usually used abundantly because of two erroneous beliefs and a common fault in surgical technique. The first mistaken belief is that the larger sizes of sutures necessarily contribute the most strength to the wound, or in other words, it is not known how to obtain maximal strength with the least amount of suture material. The second is the erroneous belief that the complications of wound healing, such as disruptions, hematomas, and secondary hemorrhages, are avoided by suturing tissues as securely as possible in the manner used to tie inanimate objects. The fault in surgical technique is hurry.

The maximal strength of a wound is obtained with a minimal amount of suture material by suturing fasciae only, and by placing these sutures in such a manner that they pull at right angles to the major alinement of tissue fibers. This maximal strength cannot be reduced in amount unless the sutures employed have a knot or thread strength less than size No. 0, nor can it be increased by using sutures of larger sizes. In either case the holding power of the tissues for the sutures determines the strength of the wound. In tissues other than fasciae, finer sizes of catgut should be used. Because the holding power of the tissue for the suture determines the strength of the wound, the wound is strengthened by an increase in the number of sutures employed rather than in the size of the suture. However, no additional strength is provided by placing the sutures closer together than 1 centimeter (3).

Maximal strength of the wound is maintained by the use of interrupted sutures. If one interrupted suture breaks or sloughs out of the tissues, the others carry on their intended function. On the other hand, if a continuous suture is used, the entire strength of the wound is jeopardized when a break occurs anywhere along its length.

#### COMPLICATIONS OF WOUND HEALING

Contrary to current belief, complications of wound healing are really reduced in number by decreasing the size of the catgut used within the limits stated. Increasing the quantity of catgut used and placing it needlessly in tissues where no important mechanical advan-

tages result, tend to increase the amount of edema and exudative reaction, cause necrosis of tissue, decrease the holding power of the tissue for the sutures, weaken the thread strength of the catgut, and finally weaken the wound. Use of the larger sizes of catgut predisposes to wound infection, not only because the larger sizes provide a greater amount of foreign body in the wound, but also because the technique which is employed with them inevitably causes greater tissue destruction and provides a soil for the growth of bacteria. Hematomas become almost unknown when the finer sizes of catgut are used.

To prevent disruption of the laparotomy wound, the key tissue to suture properly is the posterior sheath of the rectus muscle. In the longitudinal incision of the anterior abdominal wall, the fibers of the posterior sheath are cut at right angles. Sutures placed in these cut edges pull out parallel to the fibers, and are consequently held insecurely. This sutured union, being the first defense against disrupting forces, separates in the first few days after operation and causes the disruption or a post-operative herniation depending on whether the outer layers give way also. To increase the strength of this layer, a mattress type of suture should be employed.

Hurry in suturing tissues necessitates the use of large needles which will not break and large sizes of catgut (Nos. 2 and 3) in long continuous strands. Large bites of tissue, i.e., greater than  $\frac{1}{2}$  centimeter, are taken and there is a greater tendency to tie tighter. In other words, the suture technique is the exact opposite of that employed with fine catgut and therefore results in a greater number of wound complications.

#### HOW TO PREVENT BACTERIAL CONTAMINATION OF CATGUT

Although sterile when placed on the operating table, catgut sutures often become contaminated with bacteria by the time they are tied in the tissues. These bacteria come from the air, and more commonly from the tissues and blood of the wound. Regardless of the type of antiseptic used, bacteria can be grown with surprising regularity from the first blood entering the

wound after the skin has been cut. Whether the tissues can resist these relatively harmless bacteria depends in part on the amount of foreign body present in the wound. All sutures are foreign bodies and, therefore, a reduction of the quantity of suture material used decreases the possibility that the bacteria will gain a foothold. The minimizing of trauma caused by their insertion decreases the amount of contused tissue present, and contused tissue is not only a foreign body but a growth medium for the bacteria, thereby predisposing to infection. Contact with exposed skin, repeated soiling with serum such as occurs when ligatures are taken from a spool, and contact with linen or instruments which have been in the operative field are all sources of contamination which should be avoided during an operation. In too many instances improper sterilization of catgut during preparation is given as the cause of wound infections, whereas the faults are actually those of surgical technique.

#### CATGUT AND CONTAMINATED WOUNDS

Catgut is overwhelmingly the suture of choice in contaminated wounds. Kocher, in spite of his preference for silk for clean wounds, did not hesitate to use catgut in contaminated wounds. Halsted never discussed this point in any of his writings, except to say that if an infection developed with silk there would probably be little trouble if the silk were fine enough. Only Shambaugh and Dunphy have come out strongly for the use of silk in contaminated wounds on the basis that the duration of infection with silk is no longer than with catgut. However, in many of the cases repaired with silk, the sutures were mechanically removed and, unfortunately, offending silk stitches are not always available for mechanical removal.

When catgut is used to repair a freshly contaminated wound made to drain an infected focus, such as an abscess in the peritoneal cavity, the spirit of "contaminated anyway" usually dominates the technique. Only infrequently is a half-hearted attempt made to have the catgut reach its final location with a minimal amount of bacterial contamination. Instead, the sutures are used to inoculate the

bacteria deep into tissues where the ordinary seepage along a drainage tract would never place them. To prevent this catastrophe, four suggestions are offered for the management of this type of wound: (1) The edges of the wound should be well walled off with laparotomy pads before the peritoneum is opened. (2) The pus should be removed by suction and not allowed to flow over the wound edges. (3) The drain should be placed at one end of the wound. (4) After the peritoneum is closed, the wound is irrigated, débrided, redraped, and treated just like any contaminated traumatic wound. With this technique, catgut sutures can be inserted into the tissues with little or no bacterial contamination.

#### THE OBJECT OF THE USE OF CATGUT

The object of all suturing is to allow the cells to regenerate between the cut edges and thus restore the continuity of the wound. The work of Ravdin, Thompson, et al (7), showing that fibroblasts appear late, proliferate slowly, and that the wound disrupts whether sutured with catgut or silk in the presence of hypoproteinemia, illustrates the ultimate uselessness of sutures if cells do not regenerate. Ingalls, et al (5), have shown that wounds heal poorly and disrupt regardless of the type of suture material used if there is a C-avitaminosis because fibroplasia is distorted. The failure of cells to regenerate properly, therefore, should not be caused by the sutures themselves. The object of their use is thereby nullified. Infection in wounds, necrotic tissue, and excessive amounts of foreign bodies retard the growth of cells, and all these changes can be produced by sutures. The size of the suture, and its method of use are the important factors to be considered. "Think of the cells" is the best of all possible maxims for the use of sutures, and more attention should be given to their use to improve the results of wound healing.

#### SUMMARY

This article is purely a plea for the better use of the catgut suture. The following points have been emphasized.

1. The selection of plain or chromic catgut is determined by the rate of healing of the tissue in which the suture is to be used.

2. Catgut is tolerated poorly in skin, subcutaneous fat, mucous membranes, and muscles.

3. Maximal strength of the wound is obtained by the use of sutures in the fascia when they pull at right angles to the fibers. Maximal strength is maintained by the use of interrupted sutures.

4. Complications of wound healing are reduced in number by decreasing the size of the catgut used. No catgut suture larger than No. 0 need be used in fascia; No. 000 in muscle, No. 0000 in subcutaneous fascia, and No. 00000 in mucous membranes. In order to prevent wound disruption and postoperative hernia, the key tissue to be sutured in the laparotomy wound is the posterior sheath of the rectus muscle.

5. In the repair of clean wounds, catgut sutures are often needlessly contaminated by unsuspected faults in surgical technique.

6. Whether tissues will resist bacterial infection or not depends on the amount of foreign body and necrotic tissue present in a wound, and since all sutures are foreign bodies and are capable of producing necrotic tissue by their misuse, a reduction in the quantity of catgut employed and the adoption of the careful tech-

nique required for the finer sizes decrease the opportunity for infection.

7. In contaminated wounds catgut is the suture material of choice, but seldom is an effort made to prevent its contamination. Four suggestions are offered to prevent contamination of the suture in the repair of the wound made clean to drain an infected focus in the peritoneal cavity.

8. The object of all suturing is to allow cells to regenerate. All types of sutures are useless when cells fail to regenerate for other reasons, but certainly neither the sutures nor their method of use should be made the cause of this failure.

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# THE PROPHYLACTIC IMPLANTATION OF SULFANILAMIDE IN CLEAN OPERATIVE WOUNDS FOR THE REDUCTION OF POSTOPERATIVE INFECTIONS

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**M**OST surgeons will agree with the statement that every operative incision is potentially an infected wound. This is one of the unsolved problems of surgery, and the possibility of postoperative infection not infrequently causes the surgeon to advise against an operation which, in his opinion, would be beneficial to the patient but is hardly worth the risk involved. This is particularly true in the treatment of fractures when the surgeon is often content with a fair result obtained by manipulative means or traction when by open operation he could have obtained a more perfect result with much less effort.

So important is the question of postoperative infection that the American College of Surgeons in 1940 devoted one symposium to the subject (Meleney, 9) and another symposium to sterilization and aseptic operative room technique (Cutler, 1). We do not know just what percentage of our own clean operative wounds have become infected in the past. We can recall surgical tragedies in which the result of an apparently satisfactory operation was ruined by infection, and in one instance the patient died. We believe that between 1 and 2 per cent of our clean operative wounds have developed an infection sufficiently serious to cause a portion of the wound to be opened and drained. It is probable, however, that the percentage is higher, as Meleney (8) states that impressions in regard to the incidence of postoperative infections are woefully inaccurate.

Not only do infections occur, but in our experience attempts to trace the source of the infection have nearly always resulted in failure. An exception was on January 14, 1932,

when both of 2 clean cases in which operation had been done the same morning became infected. One was a knee from which a semi-lunar cartilage was removed and the other was a patient with Paget's disease in whom a long section of the tibia was removed for the relief of intractable pain. In each instance the infecting organism was a hemolytic streptococcus and the day after the operation a member of the operating team entered the hospital with a streptococcal throat and the organisms from the wound and from the throat seemed to be identical. At that time, folded gauze masks were used. As a result of that experience, large heavy muslin masks were adopted and during the past few years these have usually contained a sheet of cellophane and have been fitted with a strip of aluminum which is bent over the bridge of the nose. However, in spite of this improvement in the type of masks used, we have still had occasional postoperative infections.

As a result of a careful 9 year study, the surgical service of the Presbyterian Hospital in New York City was able to reduce the incidence of postoperative infections from 14 per cent in 1925 to 4.8 per cent in 1933. It is to be noted that of the patients operated upon in 1925, 4 per cent developed serious infections and 10 per cent developed trivial infections, while in 1933 1.1 per cent developed serious infections and 3.6 per cent developed trivial infections. Meleney (8), in his report of this study, indicated that the work would be continued and in his second report (Meleney, 9) it is shown that in 1939 the incidence of serious infection was 0.6 per cent and of trivial infection was 2.6 per cent. Meleney suggests ways and means of minimizing postoperative infections and emphasizes particularly sufficient autoclaving and proper masking of the nose

and mouth of the operating personnel. He also lays stress on the advantage of fine silk over catgut as suture and ligature material and mentions the fact that the operating room personnel have become infection-conscious. It is our belief that this last is probably the most important single factor in the reduction of postoperative infection.

Hart, in a brief review of his experience with the use of ultraviolet radiation as a method of sterilizing the air in the operating room at the Duke Hospital, stated that as a result of this change in technique the incidence of infection in that hospital has been reduced from an average of 4 per cent in clean primary incisions of small magnitude to considerably less than 1 per cent in a series of extensive operations in which the ultraviolet radiation was used.

It is evident from Hart's report and from his numerous papers on the subject that he believes that most operative infections are due to contamination of the air in the operating room, and he attributes the reduction in postoperative infection to the relative sterilization of this air and to the killing of bacteria which may have settled on the dressings and instruments or on the surface of the wound. From his writings there is no question but that the introduction of ultraviolet radiation into the operating rooms has been followed by improvement in the results obtained by the surgeons in that hospital. However, here, too, the fact that the presence of the radiation has rendered the surgical staff infection-conscious must be considered and may be a factor in the reduction of the number of postoperative infections. At any rate, the results at the Presbyterian Hospital as reported by Meleney and at the Duke Hospital as reported by Hart with radiation are comparable, although they attribute their improvement in results to entirely different procedures.

On May 26, 1939, we performed a cup arthroplasty of the hip on a patient with bony ankylosis of both hips. Infection developed in the wound and eventually the cup was removed. The final result was a recurrence of the ankylosis in a somewhat more satisfactory position. At that time we had been impressed by the results obtained by Jensen, Johnsrud

and Nelson in the treatment of compound fractures by the implantation of sulfanilamide powder in the wound and we had used this method in compound fractures and other contaminated or potentially infected wounds. We had also performed a number of animal experiments which had convinced us that the presence of the sulfanilamide did not materially interfere with the healing of the soft tissues of the wound and that it did not appreciably interfere with the union of fractures in experimental animals. (Key et al., 4, 5, 6, 7).

As a result of the experience with this arthroplasty, we began implanting sulfanilamide in the wounds of our more serious operative cases. The results following the implantation of sulfanilamide in the larger operative wounds were so satisfactory that we gradually increased the frequency with which we have used the drug until at the present time sulfanilamide powder is routinely implanted in all of our clean operative wounds before the wound is sutured.

Since May 26, 1939, only 3 patients on whom one of us (J. A. K.) has operated and sutured the wound have developed a postoperative infection. Two of these were in wounds which were not really clean but were in old infected compound fractures which were operated upon relatively soon after the sinuses had closed. These developed low grade infections about 10 days after the operation and drained for a few weeks and then healed. They were the only two of a group of cases operated upon at the Missouri Pacific Hospital which developed an infection and are not included in this series of 150 patients who were all operated upon at the Barnes and the Jewish Hospitals.

Of the patients operated upon at the Barnes Hospital, there were no postoperative infections in the usual sense of the term, but the third case mentioned occurred in a boy (Case 82, Table I) 4 years of age from whom a large lymphangioma had been removed from the anterior and mesial portions of the thigh. The wounds healed by primary intention and the sutures were removed and a pressure dressing was applied. The boy was discharged to his home in Springfield, Illinois, on the tenth day after the operation. There the dressing

was removed and he developed a swelling on the front of the thigh and fever. He returned to the hospital 8 days after discharge with a large fluctuant swelling on the front of the thigh. A hemostat was pushed through the paper-thin operative scar and about 100 cubic centimeters of clear fluid was evacuated. Sulfanilamide powder was placed in the cavity and the patient made an uneventful recovery and returned to his home 10 days later.

In another patient (Case 61, Table I) the lower portion of the wound in the back was opened on the third postoperative day because an infection was feared. No infection was present and it was determined later that an infection and retention of urine in the bladder accounted for the patient's temperature. This patient later developed a bed sore which led to a low grade infection in the wound.

Among the patients operated upon at the Jewish Hospital during this period, there have been no postoperative infections or complications such as the 2 mentioned.

Naturally, the question arises as to whether or not the local implantation of sulfanilamide powder in the wound is dangerous to the patient. In order to answer the various objections which have been raised to the method, we are, in this paper, recording observations on 150 almost consecutive operations of various types. These operations were all performed by one surgeon (J. A. K.). They were performed in two hospitals under conditions which exist in the general surgery operating room in the average good hospital. They were performed with frequently changing personnel of assistant residents, internes, and nurses. The air in the operating room was not conditioned and no appreciable change in technique has been made from that followed in the past. For the most part, silk was used for ligatures and sutures. The surgery was as atraumatic as was consistent with the skill of the operator. Care was taken not to tie the sutures too tightly and to leave as few buried sutures and ligatures as was consistent with adequate closure and hemostasis. In some instances the skin has been closed with catgut when prolonged immobilization in a plaster cast was indicated and when it was not desirable to change or to cut a window in the plaster. In

other instances sutures of chromic catgut have been placed where it was deemed a disadvantage that the sutures be permanent, as in closing the muscles after a spinal fusion. The skin has been protected by skin towels in about half of the cases; that is, in most of the major cases in which the application of the towels would not interfere with the operation. The skin preparation has been as follows:

The patient entered the hospital the day before the operation in most instances. The extremity was scrubbed with soap and water and shaved. It was then scrubbed with alcohol. In certain instances it was painted with tincture of merthiolate or mercresin the day before the operation. No sterile dressing was applied. After the patient had been placed on the operating table, the field of the operation was scrubbed with alcohol or ether, and painted with tincture of merthiolate or tincture of mercresin.

In Tables I and II are listed a series of 150 almost consecutive clean operations in which sulfanilamide powder was implanted in the wound. The maximum rise in temperature after the operation, the character of healing of the wound and the length of stay in the hospital after the operation are given in the tables. It is to be noted that the hospital stay varies greatly, even in operations of the same type. This is because most of these patients were private patients, and their stay in the hospital was regulated largely by their economic status. For instance, Case 66 and Case 69 were 2 patients operated upon on the same day for nonunion of fracture of the hip, by McMurray's oblique osteotomy. One patient went home on the tenth day after the operation in a plaster-of-Paris cast and convalesced at home. The other patient remained in the hospital for 118 days, until she was walking well on crutches. Both wounds healed *per primam* with no complications.

#### ANALYSIS OF CASES

*Rationale of the procedure.* When sulfanilamide powder is placed in the wound, this powder becomes dissolved in the fluid which collects in the wound and this fluid is then a saturated solution of the drug, if an excess of the drug is available, and 1 gram of the drug

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TABLE I.—RÉSUMÉ OF 110 CASES IN WHICH SULFANILAMIDE WAS PLACED IN WOUNDS AFTER OPERATION—BARNES HOSPITAL

Case No.	Hospital No.	Diagnosis	Operation	Anesthesia	Post-operative temperature degrees C.	Post-operative days in hospital	Healing
1	75904	Chronic sacro-iliac strain, left	Sacro-iliac fusion	G	38.1	15	P
2	56360	Healed fracture tuberosity os calcis	Removal of nail	L	37	1	P
3	75870	Disorganization of hip joint left	Shell operation	G	38	11	P
4	75467	Chronic arthritis right sternoclavicular joint	Biopsy of clavicle and joint	G	37.6	10	P
5	68553	Metastatic fibrosarcoma right inguinal nodes	Excision lymph nodes	G	37.2	6	P
6	75951	Psoriasis arthropathica	Synovectomy right knee	G	37.6	11	P
7	76604	Osteoid osteoma of tibia	Excision	G	37.8	7	P
8	75761	Deformity of left foot, post-traumatic	Reconstruction of foot	G	37.2	8	P
9	73406	Old fracture vertebrae, 4th and 5th lumbar	Lumbosacral fusion	L	38.5	19	P
10	75177	Diabetes mellitus. Suppurative arthritis left knee. Arteriosclerotic gangrene left foot	Midhigh amputation	G	38.1	18	P
11	75664	Bilateral hallux valgus	Silver operation. Bilateral	L	37.8	9	P
12	78382	Paralysis of ulnar nerve	Ulnar nerve transposition	G	37.4	3	P
13	78431	Subluxation of navicular and lunate bones of hand	Removal of navicular and lunate bones	G	37.5	3	P
14	79125	Bilateral hallux valgus	Keller operation	L	37.8	12	P
15	79189	Comminuted fracture dislocation right humerus	Open reduction and wiring	L	37.9	8	P
16	79261	Torn internal semilunar cartilage	Excision of cartilage	G	37.8	6	P
17	79431	Fracture of ulna and radius, left	Open reduction and wiring	G	38	8	P
18	81852	Comminuted T fracture of humerus	Open reduction and wiring	G	38.1	30	P
19	82696	Fracture of olecranon	Open reduction and wiring	G	37.5	9	P
20	82528	Traumatic arthritis ankle joint, left	Arthrodesis of ankle	G	38	15	P
21	82415	Subdeltoid bursitis	Excision bursal lining	G	37.5	5	P
22	79491	Fracture of ulna and radius, left	Open reduction	L	37.5	8	P
23	80266	Hallux valgus, bilateral	Keller operation	G	38	5	P
24	80318	T fracture of humerus	Open reduction and wiring	G	37.4	20	P
25	32994	Old osteomyelitis of tibia, right	Midleg amputation	L	37.5	7	P
26	80455	Loose body, left knee joint	Removal of loose body	G	37.4	15	P
27	80499	Fracture olecranon, left	Open reduction and wiring	G	37.4	15	P
28	68359	Old osteomyelitis, left tibia	Amputation left leg at knee	G	38.1	10	P
29	81023	Chondrosarcoma clavicle, right	Removal of clavicle	G	38	16	P
30	A4824	Osteoid osteoma of tibia	Excision osteoma of tibia	G	37.8	4	P
31	68889	Osteoid osteoma of fibula	Excision, osteoma of fibula	G	37	32	P
32	61156	Chronic osteoarthritis of hip	Cup arthroplasty	L	38	12	P
33	80310	Coccygodynia. Pilonidal cyst	Excision of coccyx. Excision of cyst	G	38	16	P
34	46780	Familial osseous atrophy of feet with osteomyelitis of right foot	Amputation, right leg	G	39.4	42	P
35	A4829	Old pyogenic arthritis, right knee	Arthroplasty of knee	L	38.4	21	P
36	84331	Spondylolisthesis	Lumbosacral fusion	G	37.8	5	P
37	84375	Fracture tibia and fibula	Open reduction and nailing condyle Excision external semilunar cartilage				

P, primary healing. G, general and L, local anesthesia.



TABLE I—RÉSUMÉ OF 110 CASES IN WHICH SULFANILAMIDE WAS PLACED IN WOUNDS AFTER OPERATION—BARNES HOSPITAL—Continued

Case No	Hospital No	Diagnosis	Operation	Anesthesia	Post-operative temperature degrees C	Post-operative days in hospital	Healing
38	84547	Hallux valgus	Keller operation	L	37.2	10	P
39	84460	Compound and simple comminuted fracture of tibia and fibula	Open reduction and plating	G	37.5	12	P
40	89158	Tuberculosis of spine	Spinal fusion	L	38.4	17	P
41	84130	Osteochondritis of tibial tubercle	Drilling of tubercle	L	37.6	1	P
42	83935	Fracture greater tuberosity of humerus	Open reduction and nailing	L	37.8	14	P
43	84905	Flail elbow	Revision of elbow	G	38.6	2	P
44	83301	Fracture of olecranon	Open reduction and wiring	G	37.3	5	P
45	65118	Traumatic synovitis left knee	Exploration of knee	G	38.5	13	P
46	84689	Fracture of olecranon	Open reduction and wiring	G	37.9	5	P
47	A3977	Comminuted fracture of humerus	Open reduction and wiring	G	38.3	6	P
48	A9033	Chronic hyarthrosis, right knee	Synovectomy	G	38	5	P
49	A8570	Internal derangement of left knee	Excision both semilunar cartilages and of exostosis of tibia	G	37.6	14	P
50	85350	Fracture of radius and ulna	Open reduction and wiring	G	37.8	2	P
51	86029	Hallux valgus with hammer toe, bilateral	Excision 4 metatarsal heads and Keller operation	G	37.9	10	P
52	86105	Old traumatic diastasis of ankle joint	Reconstruction of ankle and wiring malleoli	G	37.8	12	P
53	76420	Contracture of forearm muscles	Tenolysis of flexor tendons	G	38.1	5	P
54	85522	Fracture of olecranon	Open reduction and wiring	G	38.5	5	P
55	71762	Chronic anterior subluxation of shoulder	Tendon suture to humeral head and plication of capsule	G	39.7	9	P
56	85221	T fracture of humerus	Open reduction and wiring	G	38.1	4	P
57	85164	Fracture head of radius	Removal head of radius	G	37.8	3	P
58	75051	Psoriatic arthritis of knee left	Synovectomy	G	38	9	P
59	A9646	Osteoarthritis of hip	McMurray osteotomy of femur	G	37.8	85	P
60	A10098	Transverse comminuted fracture neck of humerus	Open reduction and wiring	G	38	16	P
*61	A10300	Spondylolisthesis	Lumbosacral fusion	L	39.8	24	P*
62	A9025	Comminuted fracture, right patella	Excision of patella	G	37.8	31	P
63	71067	Hallux valgus, bilateral	Operation for hammer toe and Keller operation bilateral	G	37.4	9	P
64	83364	Chronic subdeltoid bursitis bilateral	Excision of bursal lining bilateral	L	37.5	7	P
65	84440	Osgood Schlatter's disease bilateral	Drilling of tibial tubercles	L	37.6	1	P
66	82384	Old fracture of femoral neck with nonunion	McMurray osteotomy of femur	G	37.9	10	P
67	83508	Chronic tenosynovitis of thumb	Lysis of adhesions and opening of tendon sheaths	L	37.2	2	P
68	83942	Joint mice elbow posttraumatic	Exploration of elbow with removal of joint mice	G	38	0	P
69	82177	Fracture of femoral neck with nonunion	McMurray osteotomy of femur	G	38	113	P
70	78431	Osteochondroma of sternum	Excision	L	37.3	4	P
71	65 11	Calcification over trochanter Spur on calcus	Excision	G	38.4	9	P
72	74141	Old tuberculosis of knee	Arthrodesis of knee	G	37.8	18	P
73	77520	Old gunshot wound of foot	Triple arthrodesis of foot	G	38	6	P

P, primary healing \*complications explained in text

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 TABLE I.—RÉSUMÉ OF 110 CASES IN WHICH SULFANILAMIDE WAS PLACED IN WOUNDS  
 AFTER OPERATION—BARNES HOSPITAL—Concluded

Case No.	Hospital No.	Diagnosis	Operation	Anesthesia	Post-operative temperature degrees C.	Post-operative days in hospital	Healing
74	81730	Coccygodynia	Excision of coccyx	G	37.4	10	P
75	79218	Progressive muscular atrophy with unstable ankle	Triple arthrodesis and Campbell block	G	38	14	P
76	81295	Coccygodynia	Excision of coccyx	G	38.2	8	P
77	P1394	Volkman's contracture	Reconstruction of forearm	G	37.8	9	P
78	P1554	Congenital torticollis	Lengthening of sternomastoid and deep fascia	G	38.5	2	P
79	Q2451	Cyst, neck of femur	Osteotomy	G	38.4	9	P
80	Q2229	Fracture, head of radius	Open reduction	G	38.4	2	P
81	Q1014	Congenital torticollis	Lengthening of sternomastoid and deep fascia	G	37.6	5	P
*82	Q1716	Lymphangioma of thigh	Excision of tumor	G	38	10	P*
83	J1603	Spastic paralysis	Popliteal neurectomy. Lengthening heel cord. Triple arthrodesis	G	39.2	7	P
84	K1272	Talipes equino varus	Stabilization of foot. Lengthening heel cord	G	38.6	9	P
85	G1453	Congenital pseudoarthrosis	Double bone graft, tibia	G	38.1	7	P
86	J2243	Old fracture, right femur	Epiphyseal arrest at knee, left	G	37.8	8	P
87	Q888	Osteochondroma and deformity of radius	Osteotomy of radius and ulna	G	38.4	3	P
88	81034	Fracture of leg with nonunion	Step operation	L	38.2	14	P
89	70148	Fracture of femur with nonunion	Onlay graft to femur	G	38	37	P
90	78714	Fracture of femur	Open reduction and wiring	G	38.4	31	P
91	77795	Internal derangement of knee	Excision of semilunar cartilages of knee	G	38	11	P
92	81752	Hallux valgus, bilateral, with hammer toes	Operation for hallux valgus and hammer toes. Lengthening heel cord	G	37.8	8	P
93	77075	Internal derangement of knee joint	Excision of semilunar cartilages and reconstruction of both lateral ligaments	G	38.6	11	P
94	77589	Old fracture femoral neck	Colonna reconstruction of hip	G	38.4	44	P
95	76711	Old fracture femoral neck	Colonna reconstruction of hip	G	37.9	50	P
96	77637	Fracture of head of radius	Resection of head of radius	G	38.3	3	P
97	72619	Chronic sacroiliac strain	Sacroiliac fusion	G	38.4	12	P
98	75626	Scar of deep muscles of thigh	Removal of scar tissue and lysis of adhesions	G	37.9	11	P
99	75570	Congenital dislocation of hip	Shelf operation	G	38.5	6	P
100	45783	Chronic olecranon bursitis	Excision of bursa	L	37.3	1	P
101	84439	Arthritis, left ankle joint	Arthrodesis of ankle	G	38.1	14	P
102	B197	Subdeltoid bursitis, right	Excision of bursa	L	37.5	2	P
103	B242	Recurrent dislocation of shoulder	Modified Nicola operation	G	38.3	17	P
104	B581	Sarcoma of clavicle	Excision of clavicle and tumor	G	38	10	P
105	75837	Interdigital clavus	Excision of exostosis and osteotomy of phalanges	L	37.4	3	P
106	84449	Fracture of femoral neck	Nailing of hip	L	38.2	19	P
107	B328	Fractured patella, old	Wiring and lengthening of quadriceps	G	38.4	10	P
108	B221	Fracture of femoral neck	Nailing of hip	G	38.6	28	P
109	E36903	Old septic hip	McMurray's osteotomy and transplant of trochanter	G	38.5	19	P
110	B287	Subdeltoid bursitis	Excision of subdeltoid bursa	L	37.6	3	P

P, Primary healing; \*Complications, explained in text.

TABLE II—RÉSUMÉ OF 40 CASES IN WHICH SULFANILAMIDE WAS PLACED IN WOUND AFTER OPERATION—JEWISH HOSPITAL

Case No	Hospital No	Diagnosis	Operation	Anesthesia	Post operative temperature degrees F	Post operative days in hospital	Healing
1	250072	Tear internal semilunar cartilage	Excision of cartilage	G	100.2	11	P
2	213403	Recurrent dislocation of patella	Hitchcock operation	G	100	14	P
3	401860	Torn internal semilunar cartilage	Excision of cartilage	G	101.8	6	P
4	401870	Nonunion of tibia	Multiple drilling	L	99.4	10	P
5	401848	Fracture, left radius	Open reduction	G	100.2	2	P
6	301718	Fracture, left radius	Open reduction	G	99	4	P
7	401867	Hallux valgus, bilateral	Bilateral Keller operation	G	101	9	P
8	401863	Torn internal semilunar cartilage	Excision of cartilage	G	99.2	4	P
9	401861	Cyst of external semilunar cartilage	Excision of cartilage	G	98.8	11	P
10	401526	Nonunion of femur	Step operation	G	101	112	P
11	270033	Sciatic pain	Obel fasciotomy	G	99.8	9	P
12	262586	Old fracture of olecranon	Wire and autogenous bone peg	G	102	4	P
13	401844	Osteoid osteoma astragalus	Excision	G	100	7	P
14	262318	Subdeltoid bursitis	Excision bursal lining	G	99	7	P
15	401874	Rupture long head of biceps	Suture to coracoid	G	100	6	P
16	400602	Calcification over internal condyle of femur	Excision of calcified area	L	100.5	8	P
17	401866	Hallux valgus, bilateral	Bilateral Keller operation	L	99.5	7	P
18	401864	Sciatic pain	Obel fasciotomy	G	100	8	P
19	401862	Tear of internal semilunar cartilage	Excision of cartilage	G	101	5	P
20	402119	Tear of internal semilunar cartilage	Excision of cartilage	L	100.5	11	P
21	330590	Osteochondroma of scapula	Excision	G	99.4	5	P
22	340041	Coccygodynia	Excision of coccyx	G	99.6	7	P
23	213530	Low back and sciatic pain	Fusion, right sacrospinous and Obel fasciotomy	G	102	30	P
24	401845	Old fracture of patella	Wiring of freshened fragments	G	100.2	21	P
25	214007	Sciatic pain	Fasciotomy	G	99.2	9	P
26	213482	Fracture of patella	Excision, distal fragment and silk suture	G	101	18	P
27	213148	Spondylolisthesis	Lumbosacral fusion	L	100.4	21	P
28	214223	Fracture, radius	Open reduction	G	100.6	5	P
29	214642	Ankylosis of wrist in flexion	Osteotomy	G	99.6	2	P
30	402752	Fracture, condyle of tibia	Nailing condyle. Excision, external semilunar cartilage	G	100.6	10	P
31	215039	Internal derangement of knee	Excision, external semilunar cartilage—Maucl operation	G	101	12	P
32	215636	Old Colles fracture	Campbell's operation	G	100.5	7	P
33	215589	Tear of internal semilunar cartilage	Excision of cartilage	G	101	7	P
34	401855	Hammer toe	Hammer toe operation	L	99	1	P
35	401873	Subdeltoid bursitis	Excision of bursa	L	100.4	5	P
36	331570	Sesamoditis	Excision of sesamoids	L	100	10	P
37	401850	Fracture, right hip	Nailing of hip	L	102.4	120	P
38	250007	Fibrocystic disease of tibia	Excision of fibroma and bone chips	G	102.6	27	P
39	215045	Fracture, both bones of forearm	Open reduction and wiring	G	102.4	7	P
40	216313	Osteochondroma of tibia	Excision of tumor	G	100.5	7	P

P Primary healing

will saturate approximately 100 cubic centimeters of fluid. It has been shown by us and by other observers in the literature, which has been reviewed in a previous paper (7), that a saturated solution of sulfanilamide crystals not only inhibits the growth of strains of streptococci which are susceptible to the drug in dilute solutions, but also inhibits the growth of staphylococci and of gas bacilli and of other organisms which are not susceptible to the drug in dilute solutions. It has further been shown that the efficiency of the drug varies inversely with the number of organisms present. Consequently, in a clean operative wound which is contaminated by relatively few pathogenic organisms, the situation should be ideal for the inhibition of the growth of these organisms by the drug to a point where the defense mechanism of the patient can destroy the contaminating bacteria. The sulfanilamide powder remains in the wound for about 48 hours and it not only saturates the fluid in the wound, but it diffuses into the surrounding tissues.

In placing the powder in clean operative wounds, much less of the drug is used than is used in contaminated wounds. In the beginning some of our wounds developed an excess of serum in the wound and we believe that this was, in part, due to the presence of too much powder. As our experience with the method has increased, we have reduced the amount of the drug until now we rarely put more than 5 grams in a single wound, the amount depending upon the size of the area to be covered. The powder is sprinkled lightly over the surface of the wound just before closure and after hemostasis has been effected. When used in clean wounds, the powder is sterilized by autoclaving for 30 minutes at 15 pounds pressure and is then pulverized if lumpy, or sterile powder from ampuls is used.<sup>1</sup>

In the closure of the wound, an effort has been made to eliminate dead spaces and to avoid excessive constriction of tissues. In other words, the fact that we have used sulfanilamide in the wound has not been regarded as justification for any letting down in our surgical technique. It is to be emphasized

that the method is not infallible and that, even with the use of sulfanilamide, occasional clean wounds will become infected. As a matter of fact, we know of 4 such instances, but as we did not see any of these patients we can make no statement as to why they became infected.

Unfortunately, no statement can be made concerning the occurrence of stitch abscesses in this series. It is possible that some have occurred, but we do not recall any particular instance, nor has any notation of stitch abscesses been found in the histories which were reviewed for this paper. It is our impression that the wounds have healed firmly in approximately the same time, if not somewhat less time than occurred in similar wounds in which sulfanilamide was not implanted, and it has also been our impression that stitch abscesses have been almost, if not altogether absent. At least, we do not recall a wound in this series in which a stitch abscess occurred.

It is to be noted, however, that we have not in the past considered a stitch abscess as being a postoperative wound infection. We have considered the wound infected when the wound was opened and infected material drained from the wound. It is thus evident that we made no distinction between trivial and severe infections. It is our custom to open wounds when there is suspected infection rather than to wait until the infection becomes severe. As a matter of fact, we have, on occasion, opened wounds which were not infected, because we feared infection and would rather let the wounds heal by granulation than run the risk of a severe infection (Case 61, Table I).

The fact that all of these wounds healed by primary intention is evidence that the sulfanilamide does not seriously interfere with the healing of the wound. The question then arises as to whether or not any toxic effects are to be expected from the local implantation of sulfanilamide in the wound.

With the exception of the collection of lymph (which later became infected) in one of the wounds in Case 82, Table I, and the cystitis and a bed sore in Case 61, Table I, the only postoperative complication which occurred in any of these patients was fever. In 4 of the patients operated upon at the Barnes Hospital the temperature exceeded

<sup>1</sup>In some of our cases we used sterile ampuls donated by Eli Lilly and Company.

38.6 degrees C. and in 3 of the Jewish Hospital cases the temperature reached 102 degrees F. The fever was of short duration and there were no local signs of infection. One of the wounds (Case 61, Table I) was opened for a short distance, but no infection was found. It is possible that the sulfanilamide was partly responsible for the fever, but other than causing uneasiness to the surgeon it did no harm. On the other hand, we have seen similar postoperative elevations of temperature in patients who did not have sulfanilamide implanted in their wounds and in whom infection did not develop.

Determinations of the concentration of sulfanilamide in the blood were made on several patients on the first 3 days following operation. The concentration varied from 1 to 9.2 milligrams per cent on the first and second postoperative days and usually only a trace was present on the third day after the operation. The concentration of 9.2 milligrams per cent was present in the blood of a patient who had had 10 grams of sulfanilamide implanted in a large operative wound for exposure of the hip. Lately only 5 grams of the drug have been used for this type of operation, and this usually causes a concentration of from 2 to 4 milligrams per cent in the blood. In patients with small wounds in whom the amount of the drug was small, no determinations were made.

This series does not include patients in whom active tuberculosis was present in the operative field. One such patient developed a sinus about 3 weeks after a sacroiliac arthrodesis. Another developed a sulfanilamide rash on the third postoperative day. This lasted 2 days and then disappeared. The patient was a child 7 years old with a rather large tuberculous focus in the ilium above the acetabulum. This was cleaned out, the cavity was packed with bone chips and sulfanilamide, and the cavity was closed. The temperature rose to 103 degrees F., and the rash appeared on the third day. The child was sent home in a cast on the seventh postoperative day with a normal temperature and no rash.

It is true that sulfathiazol is more effective against staphylococci than is sulfanilamide, and for this reason it may be a more desirable

drug to use. It has the possible disadvantage that it is less soluble and tends to remain in the wound longer. We are now running a series of cases with sulfathiazol powder implanted in the wounds, and, when the number of such cases is adequate, we shall report our opinion as to the value of this drug for the prevention of postoperative infection. At present we can only say that we have had no postoperative infections in the 87 clean wounds in which sulfathiazol powder has been implanted, and in small amounts it does not appear to interfere with the healing of the wound.

#### CONCLUSIONS

1. Powdered sulfanilamide can be implanted in clean operative wounds and does not interfere with the healing of the wounds unless an unnecessarily large amount of the drug is used.

2. When used in the manner described, there is practically no danger of toxic symptoms.

3. In our hands the drug has reduced the incidence of postoperative infections; no postoperative infection occurred in over 150 consecutive wounds in which the drug was used. In several patients there were two or more wounds.

4. The drug should be sterilized by autoclaving at 15 pounds pressure for 30 minutes or by some other adequate method before it is used in clean wounds. (Sterile ampuls of the powder are on the market).

5. The drug is not a panacea and its local implantation does not warrant any relaxation in the standards of good operating room technique.

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were given. The whole course covered a period of 24 days, in which, as will be shown later, no significant pathological change of the small intestine occurred. The depth dose was calculated from an isodose curve with the measurements of the anteroposterior and lateral diameters and the configuration of the circumference of the dog's abdomen. In this way the dose given compared well with the dose in a human case, when consideration is given the difference of sizes. As a matter of fact in human beings the course of x-ray therapy was frequently extended to a month or longer because of certain local or general reactions. Therefore, the dosage given to the dog can be considered to be slightly more intensive.

In an effort to find the x-ray dosage for the dog that will not produce irreparable damage to the intestine, heavier and shorter courses were tried. In one dog, a depth dose of 2400 r was given in 12 consecutive days and at necropsy the small intestine showed many hemorrhagic and ulcerated areas in the mucosa with no important changes in other abdominal viscera. This confirmed the well established observations of Warren and Whipple (14, 18). By giving the 2400 r depth dose in 20 days, we observed only occasional small hemorrhages in the intestinal mucosa, and edema. The overlying epithelium was affected at places, showing necrosis of cytoplasm and clumping of nuclei with sloughing at the surface. Therefore we took the 24 days as the minimal period during which a depth dose of 2400 r can be safely administered.

All dogs were kept in a kennel, fed on a balanced diet, and observed for a week or more in order to make sure that they were normal. The body weight and the blood hemoglobin were determined before and after the experiment.

**Controls.** Two dogs were irradiated daily with roentgen-rays through two ports in the lower abdomen. The anterior ports alternated with the posterior ports. In 24 days a depth dose of 2400 r was given. During the course of roentgen-irradiation, the animals were observed daily as to the body weight, vigor, appetite, and stool. Twenty-four hours after the last dose, the animal was killed and the

abdominal viscera were examined. The entire small intestine was examined for change in the serosa as well as in the mucosa. Photographs were taken of the mucosal surfaces. Representative sections were made from the duodenum, jejunum, and ileum. They were fixed in Zenker's solution and studied microscopically.

One dog was given a daily therapeutic dose of 30 cubic centimeters of a 2.5 per cent solution of ferrous sulfate for 24 days and then sacrificed to determine whether there was any change of the intestinal mucosa due to the drug alone. Another dog was treated similarly with 30 cubic centimeters of a 20 per cent solution of ferric ammonium citrate. In the following experiments in which the iron preparations were given in conjunction with roentgen-irradiation, the same dosage was employed. In the light of the experimental data and clinical results in the study of iron metabolism (6, 7), 0.75 gram of ferrous sulfate or 6 grams of ferric ammonium citrate administered daily is considered to be therapeutically adequate for the treatment of iron-deficiency anemia in man.

**Experiments.** Two dogs were given doses of the solution of ferrous sulfate and roentgen-irradiation daily as described. At the end of the irradiation course the dogs were killed and the abdominal viscera, especially the small intestine, were examined macroscopically and microscopically.

Two other dogs were irradiated and given the solution of ferrous sulfate as above, but were sacrificed for pathological examination 8 weeks after the completion of the treatment. This was to allow for the appearance of late effects or to see possible signs of recovery of any intestinal lesion that might be produced by the treatment.

Another series of 4 dogs was likewise irradiated but fed on a solution of ferric ammonium citrate.

In all these experiments, a stomach tube was used for feeding and the dose of the iron compound was completely ingested. During the roentgen-irradiation a plaster cast was put on the animal with windows corresponding to the irradiated fields over the lower abdomen. This made the management of the animal more convenient and irradiation more accurate.

TABLE I.—ANALYSIS OF EXPERIMENTS

Dog No.	Weight before treatment in kgm.	Weight after treatment in kgm.	Hgb. before treatment in grams per cent	Hgb. after treatment in grams per cent	Antero-posterior diameter of abdomen in cm.	Lateral diameter of abdomen in cm.	Daily skin dose in r through 2 ports	Daily depth dose in r	Days of treatment	Total depth dose in r	Ferrous sulfate 0.75 gm. daily	Ferric ammonium citrate—6 gm. daily	Disposal
1	13.5	14.1	13.6	9.6	15.0	9.5	218.6	100	24	2400			Killed at the end of treatment
2	13.5	13.2	12.2	9.4	15.0	8.5	215.0	100	24	2400			Killed at the end of treatment
3	9.8	10.3	11.5	11.0					24		yes		Killed at the end of treatment
4	9.0	9.6	11.6	13.3					24			yes	Killed at the end of treatment
5	10.6	9.5	13.4	10.7	9.5	7.5	162.0	100	24	2400	yes		Killed at the end of treatment
6	10.2	11.8	12.3	12.2	12.0	8.5	178.0	100	24	2400	yes		Killed at the end of treatment
7	12.7	12.0	13.0	11.8	12.8	10.0	206.0	100	24	2400	yes		Killed 8 weeks after treatment
8	9.5	10.5	14.5	15.2	11.5	10.5	189.6	100	24	2400	yes		Killed 8 weeks after treatment
9	10.6	10.1	13.4	11.0	12.0	8.0	177.0	100	24	2400		yes	Killed at the end of treatment
10	11.8	10.4	13.8	14.6	11.0	8.0	174.6	100	24	2400		yes	Killed at the end of treatment
11	11.5	11.5	12.5	10.8	10.5	8.5	178.6	100	24	2400		yes	Killed 8 weeks after treatment
12	10.1	9.8	11.3	8.6	12.5	7.0	187.8	100	24	2400		yes	Killed 8 weeks after treatment

Roentgen ray factors: 200 kilovolts 50 centimeters, skin target distance 4 ports, 2 anterior and 2 posterior.

Size of each port, 6 by 8 centimeters 8 milliamperes. Filter,  $\frac{1}{2}$  millimeter copper + 2 millimeters aluminum + 56 millimeters oil.

Half valve layer in copper, 1.145 millimeters.

The data on the control and experimental dogs are given in Table I.

#### EXPERIMENTAL OBSERVATIONS

**Controls.** Dogs 1 and 2 were given roentgen rays alone with a daily depth dose of 100 r and a total depth dose of 2400 r, in 24 days. During the course of irradiation their general condition was good with normal appetite and stools. At the end of the treatment, dog 1 gained 0.6 kilogram of body weight, while dog 2 lost 0.3 kilogram. Both of them developed a moderate degree of anemia. The hemoglobin of dog 1 dropped from 13.6 grams per cent to 9.6 grams per cent; that of dog 2, from 12.2 grams per cent to 9.4 grams per cent. At autopsy, the abdominal viscera appeared normal. The mucosa of the small intestine showed occasional areas of slight edema. There were no hemorrhage and no ulceration, however. The above data point to the fact that this amount of 2400 r depth dose given in 24 days was well tolerated by normal dogs

without significant clinical and pathological changes in the intestinal tract (Fig. 1).

Dog 3 was given 0.75 grams of ferrous sulfate daily for 24 days and dog 4, 6 grams of ferric ammonium citrate similarly. No roentgen-irradiation was applied. The weight of dog 3 increased from 9.8 kilograms at the beginning to 10.3 kilograms at the end of the treatment; that of dog 4 from 9.0 kilograms to 9.6 kilograms. The hemoglobin of dog 3 at the beginning of the treatment was 11.5 grams per cent and at the end, 11.0 grams per cent while that of dog 4 was 11.6 grams per cent and 13.3 grams per cent, respectively. Post-mortem examination of the abdominal viscera, especially the small intestine, showed no important changes. Thus it was clear that neither the ferrous sulfate solution nor ferric ammonium citrate alone was irritative to the intestinal mucosa. Instead, both of them improved the general condition of the dog.

*Dogs irradiated and treated with ferrous sulfate.* Dogs 5, 6, 7, and 8 were given 0.75



gram of ferrous sulfate daily for 24 days and at the same time irradiated as dogs 1 and 2. During the course of treatment, all of them showed no abnormal symptoms. The body weight and hemoglobin as shown in Figures 6 and 7, respectively, indicated no appreciable change. In other words, these animals stood the treatment well, and, when we compared the hemoglobin content of these dogs with that of the control dogs 1 and 2, it appeared that the addition of ferrous sulfate prevented or decreased the anemia produced by a prolonged course of roentgen-irradiation. The mucosa of the small intestine of dogs 5 and 6 sacrificed at the end of the treatment presented a moderate edema and some congestion. There were no hemorrhage and no ulceration (Fig. 2). Microscopically the findings were normal.

To determine if these slight anatomical lesions of the intestinal mucosa will disappear in the course of time, dogs 7 and 8 were kept and fed on normal diets for 8 more weeks. During this period they exhibited all signs of good health. When killed the intestinal mucosa appeared normal macroscopically and microscopically (Fig. 4). Evidently the slight and subclinical irritation of the intestinal mucosa produced by the feeding of ferrous sulfate and abdominal irradiation, completely recovered in the course of eight weeks.

*Dogs irradiated and treated with ferric ammonium citrate.* Dogs 9, 10, 11, and 12 were irradiated as described. In addition they were given 6 grams of ferric ammonium citrate daily throughout the entire course. They stood the treatment well without appreciable change of body weight. As shown in Figure 7 dog 10 gained some hemoglobin at the end of the treatment while the 3 others lost some. In general the hemoglobin content of the blood showed some improvement in comparison with those control-dogs, 1 and 2, but did not behave so well as those receiving ferrous sulfate during the period of irradiation treatment. This might possibly be caused by more irritation to the intestinal mucosa produced by the ferric compound itself and therefore less absorption of the substance. But it was difficult to rule out other factors such as irregularity of food intake, change of weather etc.,

which might have a similar influence. However, in these dogs no significant clinical symptoms were observed.

Pathological examination of the abdominal viscera of dogs 9 and 10 which were killed immediately after the course of irradiation showed marked edema and hemorrhages of the mucosa of the small intestine, especially in the duodenum and jejunum (Fig. 3). Microscopically, changes were evident in the epithelial cells at the tips of the villi, showing necrosis of the cytoplasm, clumping of nuclei, and superficial ulceration. In the stroma, edema and numerous areas of hemorrhage were seen. In dogs 11 and 12 which were not sacrificed until 8 weeks later, the same findings were observed in the intestinal mucosa (Fig. 5). Although one cannot say definitely from the present data how permanent the lesions may be and how much harm the animal may be done, they were of considerable significance.

#### ANALYSIS OF EXPERIMENTS

When Warren and Whipple performed their extensive work on intestinal reactions to roentgen-irradiation, the dogs were irradiated by single massive doses. In this experiment, in an attempt to arrive at a roentgen-ray dose not lethal to the dog and yet at the same time sufficiently intensive and protracted as to be comparable with the therapy of a human case of malignant pelvic tumor, we administered the 2400 r depth dose to groups of dogs in 10, 12, and 20 days. All of them exhibited unmistakable clinical signs of intoxication and pathological evidence of necrosis of cytoplasm of the epithelium, destruction of the nuclei, hemorrhages and ulceration of various degrees of the intestinal mucosa. But when the 2400 r depth dose was given in 24 days the animals stood it without clinical or pathological manifestation. This 2400 r depth dose given in 24 days may be considered to be the limit of tolerance of the small intestine of the dog to roentgen irradiation alone, and any additional effect from the use of ferrous sulfate or ferric ammonium citrate should be taken to be due to the iron compound.

In the dogs irradiated as controls there developed a moderate anemia. In the 10 other dogs receiving daily doses of iron compounds

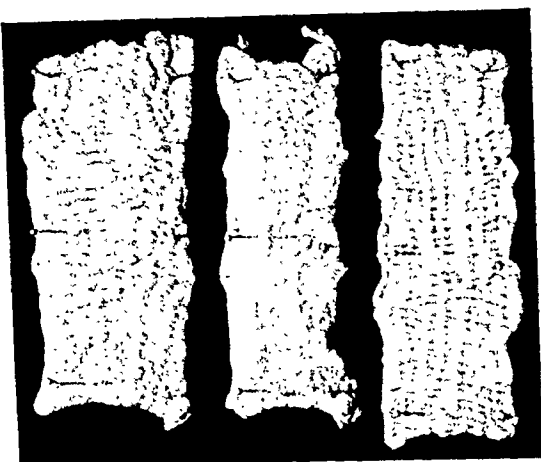


Fig. 1

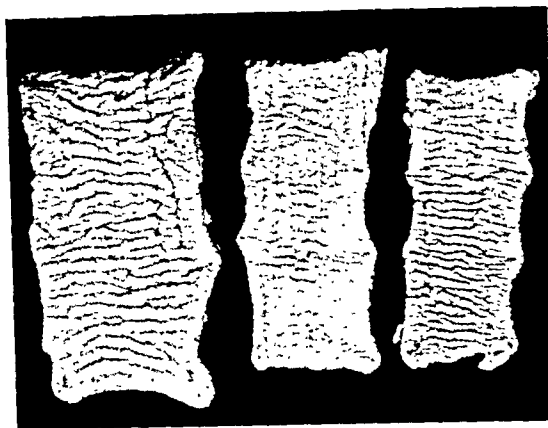


Fig. 4



Fig. 2

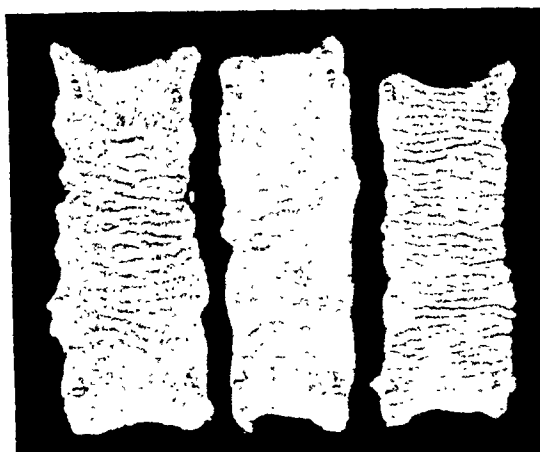


Fig. 5



Fig. 3

Fig. 1. Left, duodenum; center, jejunum; right, ileum. Intestine of dog which had received 2400 r (depth dose) in 24 days, showing no significant pathological changes.

Fig. 2. Left, duodenum; center, jejunum; right, ileum. Intestine of dog which had received 2400 r (depth dose) in 24 days as well as 0.75 gram ferrous sulfate daily, showing moderate edema and congestion.

Fig. 3. Left, duodenum; center, jejunum; right, ileum. Intestine of dog which had received 2400 r (depth dose) in 24 days as well as 6 grams ferric ammonium citrate daily, showing marked edema and areas of hemorrhage.

Fig. 4. Left, duodenum; center, jejunum; right, ileum. Intestine of dog which had received 2400 r (depth dose) in 24 days as well as 0.75 gram ferrous sulfate daily, showing normal appearance of mucosa 8 weeks after the last irradiation and medication.

Fig. 5. Left, duodenum; center, jejunum; right, ileum. Intestine of dog which had received 2400 r (depth dose) in 24 days as well as 6 grams ferric ammonium citrate daily, showing marked edema and hemorrhages 8 weeks after the last irradiation and medication.

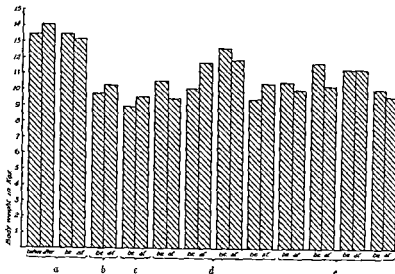


Fig 6 Chart showing the changes of the body weight of dogs after roentgen irradiation and medication with iron compounds a, Roentgen rays, 2400 r depth dose in 24 days, b, Ferrous sulfate, 0.75 gram Q D for 24 days, c, Ferric ammonium citrate, 6 grams Q D for 24 days, d, Roentgen rays, 2400 r depth dose in 24 days plus ferrous sulfate, 0.75 gram Q D for 24 days, e, Roentgen rays, 2400 r depth dose in 24 days plus ferric ammonium citrate, 6 grams Q D for 24 days

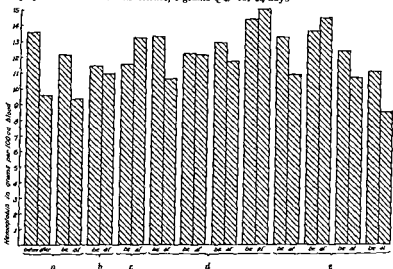


Fig 7 Chart showing the changes of the blood hemoglobin after roentgen irradiation and medication with iron compounds a, Roentgen rays, 2400 r depth dose in 24 days, b, Ferrous sulfate, 0.75 gram Q D for 24 days, c, Ferric ammonium citrate, 6 grams Q D for 24 days, d, Roentgen rays, 2400 r depth dose in 24 days plus ferrous sulfate, 0.75 gram Q D for 24 days, e, Roentgen rays, 2400 r depth dose in 24 days plus ferric ammonium citrate, 6 grams Q D for 24 days

the hemoglobin changes (Fig 7) before and after irradiation were nil or less marked.

It has been established that metallic substance lying in the path of a roentgen-ray

beam will produce secondary radiation. If the intestinal mucosa were smeared with ferrous sulfate or ferric ammonium citrate, one would expect an increase of the effect of the second-

ary rays on the tissues. This may injure the intestinal mucosa and disturb the absorption of the intestinal contents, including the iron compounds. Our experiments have been designed to find out if this additional secondary or scattered radiation from the iron substances not only in a single administration but in repeated daily doses for a prolonged period of time (3 to 4 weeks) would produce clinical symptoms and permanent pathological lesions. The fact that in 10 consecutive dogs the use of ferrous sulfate or ferric ammonium citrate had improved the anemia in at least 7 of them, spoke very strongly that absorption of iron was not significantly disturbed. Figure 7 also suggests that the regeneration of hemoglobin in those dogs treated daily with ferric ammonium citrate was not nearly so good as those treated with ferrous sulfate.

Throughout the whole experiment, we used normal dogs with normal blood hemoglobin. Were we to use subjects in which the blood hemoglobin was below normal as a result of chronic blood loss, perhaps the response to the iron therapy would be more apparent.

Pathological examinations of the viscera of those dogs irradiated and treated with ferrous sulfate showed some edema and congestion of the mucosa of the small intestine. They recovered completely in a period of 8 weeks following the abdominal irradiation. In those dogs irradiated and treated with ferric ammonium citrate one could find numerous large and small hemorrhagic patches and some superficial sloughing of the mucosa of the small intestine, more marked in the duodenum and jejunum. These lesions persisted even 8 weeks after the therapy. How long these hemorrhages in the small intestine will remain and what permanent injury may result, are questions that cannot be answered by the present experiment which had not been carried on long enough to decide. So far it was reasonable to believe that the lesions produced in the intestines of dogs fed with ferric ammonium citrate in conjunction with roentgen irradiation was not without clinical importance. As it was necessary to employ larger amounts of ferric ammonium citrate than ferrous sulfate for the same therapeutic result in the treatment of anemia due to iron deficiency (6 and

7), and the amount of secondary roentgen-rays produced is directly proportional to the mass present, no doubt the greater quantity of iron of the ferric compound was responsible for the added injury in the small intestine.

The practical application of our findings opens up a field of considerable clinical significance. The number of cases of gynecological malignant tumors associated with anemia that require roentgen-irradiation is large, and the difficulties of getting large amounts of blood for transfusion and the slow response to diet therapy alone are often disheartening in their clinical management. Although inorganic iron compounds might have been used irregularly and in short periods of time in conjunction with roentgen irradiation, no systematic and prolonged treatment has been mentioned in the literature. In our clinic we refrained from its use for a number of years for fear of an increase of undesirable radiation effect or reduction of the threshold of tolerance to radiation.

The present experiment has demonstrated that it is quite safe and definitely useful to administer ferrous sulfate to dogs during abdominal irradiation. Ferric ammonium citrate may be useful also in elevating the blood hemoglobin, but the presence of large hemorrhagic and some superficial ulcerative lesions of the small intestine with it, even after a rest of 8 weeks, suggests that it is harmful to the individual and is not desirable, until it can be proved that the intestinal lesions are not permanent and of no clinical significance.

#### SUMMARY AND CONCLUSION

1. Normal dogs irradiated through the abdomen by a protracted course of roentgen-rays for a total depth dose of 2400 r showed no clinical symptoms during the course of treatment and no pathological change of the small intestine at the end of the irradiation.

2. The daily administration of ferrous sulfate or ferric ammonium citrate in the therapeutic dose throughout the period of irradiation, tended to increase the blood hemoglobin.

3. Clinically there was no significant sign of intoxication in dogs irradiated and treated with either the ferrous or ferric compound.

4. Pathological examination of the small intestine showed a mild degree of edema and

congestion of the mucosa in these animals irradiated and treated with ferrous sulfate. These changes disappeared completely in a period of 8 weeks.

5. In those irradiated and treated with ferric ammonium citrate there was more edema and large hemorrhagic areas in the mucosa of the small intestine. These diffuse, severe hemorrhagic lesions persisted for at least 8 weeks after completion of the roentgen-irradiation.

6. The data presented serve to indicate that ferrous sulfate is definitely valuable in the treatment of the anemia as a result of chronic blood loss and it is harmless to the small intestine while the animal is undergoing abdominal roentgen-irradiation. Ferric ammonium citrate when given in its therapeutic dose is irritative to the intestinal mucosa under similar circumstances and its use is not recommended.

The authors are indebted to Dr. F. E. Whitacre and Dr. C. K. Hsieh for their suggestions and help in carrying out the experiment.

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# COMBINING SPLENECTOMY WITH TOTAL GASTRECTOMY

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**T**OTAL gastrectomy has now become an accepted surgical procedure. But a short time ago it was an operation which had been successfully accomplished only by a limited number of surgeons. The technical measures for its successful performance, however, have now been worked out and established. Total gastrectomy is being performed successfully today by many surgeons over the country. Patients upon whom total gastrectomy has been done have

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now lived long enough to establish the fact securely that without a stomach and with a loop of jejunum attached to the esophagus serving as a substitute for one, patients can maintain their weight and strength, and, with the aid of proper minerals and acids, their normal blood picture also.

When a relatively new and major surgical procedure such as total gastrectomy first appears in the surgical world, attention is largely focused upon the development of its technical steps and

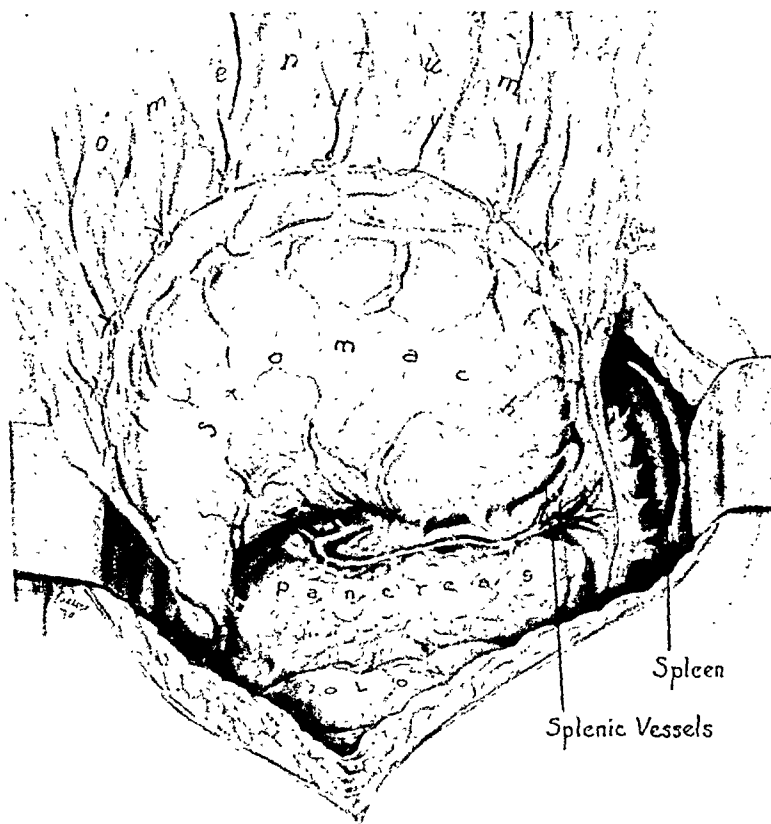


Fig. 1. In this illustration the great omentum is separated from the transverse colon and turned upward, thus exposing the lesser peritoneal cavity, the posterior wall of the stomach, the root of the gastric vessels and the splenic vessels, pancreas, and spleen. The drawing demonstrates the posterior exposure, together with the point of ligation of the splenic vessels when splenectomy is combined with total gastrectomy.

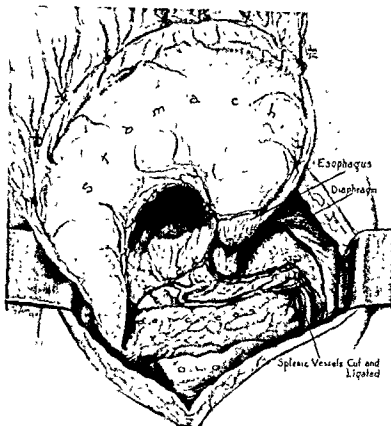


Fig. 2. In this illustration the spleen has been removed and the ample exposure of the esophagus following splenectomy is demonstrated. One can likewise see the peritoneum of the diaphragm as it extends over the esophagus, from which will be cut the apron of peritoneum with which to suspend the jejunum anastomosed to the esophagus.

associated aids, such as anesthesia, to make its mortality rate such that it can be considered as an operation which is justifiable to use in patients.

With the exception of the suggestion in this communication of the occasional employment of the additional step of splenectomy, the method of performing total gastrectomy has now been quite well established so that its mortality rate, certainly for the character of the operation, is within reasonable limits. We have now done 33 total gastrectomies with 9 fatalities. This figure includes every total gastrectomy we have ever undertaken and represents not only the mortality rate after we acquired experience with the procedure but that of the pioneer period when we were developing methods whereby the causes of some of our early failures (leakage) and fatalities could be overcome.

In the course of this experience we have five times removed the spleen together with the entire stomach, and while we do not wish to advocate splenectomy in all patients upon whom total gastrectomy is undertaken, the addition of this step will, in those cases in which the malignancy has involved the greater curvature segment opposite the hilum of the spleen, not only make the operation easier but also, by the removal of the spleen with this area, make it possible to do more complete and radical removal of the involved stomach. The addition of this step to total gastrectomy does not appear to add greatly to the hazard of the operation since in not 1 of the 5 cases in which this has been done has there been a death.

Since total gastrectomy is an operation which will be reserved almost entirely for those patients either with a linitis plastica type of carcinoma of the stomach in which gross glandular metastases



Fig. 3. Totally removed stomach together with all of the omentum and the attached spleen. The carcinoma of the stomach was of the linitis plastica type.



Fig. 4. Another specimen showing the total removed stomach with omentum, together with the attached spleen. Carcinoma of stomach was of linitis plastica type.

are so often lacking or with complete involvement of the stomach by leiomyosarcoma which is of such low grade of malignancy, it is quite desirable, we believe, to remove the entire omentum with the stomach as has been advocated by so many European surgeons writing on subtotal gastrectomy for malignancy. Removal of the entire omentum by separating it from its high attachment to the transverse colon makes it possible to remove with the stomach numerous lymph nodes in the gastrocolic omentum into which extensive carcinoma of the stomach so frequently metastasizes. Not only does the removal of the entire omentum make it possible to do a more extensive removal of gland-bearing areas with total gastrectomy but the addition of this technical step decidedly simplifies the removal of the stomach itself. As the omentum is detached from the colon and turned upward and the lesser peritoneal cavity is opened so that when the omental attachment to the colon is completely freed, the blood supply of the stomach and spleen becomes clearly visualized (Fig. 1). With this exposure of the stomach turned upward, the gastric artery with its branches comes plainly into view and the splenic vessels as they pass to the hilum of the spleen appear directly under the eye. If because of extension of the disease, because of troublesome bleeding from the vasa brevia vessels running between the greater curvature of the stomach and the spleen, it seems that a better exposure of the

lower end of the esophagus can be obtained, the splenic vessels may be ligated as trunks at this point. All of these three points have at times in our cases influenced us toward adding the operation of splenectomy to that of total gastrectomy. Four of the operations of total gastrectomy combined with splenectomy have been performed by me and one by Dr. Marshall, and we both have been impressed with the fact that with the addition of this procedure the operation has been made decidedly easier.

With the omentum completely freed from the colon and with the splenic vessels safely ligated, the parietal peritoneum outside the spleen is incised and the spleen is mobilized inward. Its pedicle can now be clamped distal to the ligature of the splenic vessels and the vascular splenic pedicle cut. This leaves the spleen attached to the upturned stomach by the vasa brevia vessels, and the large vacant area previously occupied by the spleen provides a surprisingly advantageous exposure of the left half of the diaphragm with the left lobe of the liver attached to it. With severing of the avascular attachment of this left lobe of the liver from the diaphragm, the lower end of the esophagus as it passes through the diaphragm and joins the stomach can be brought under direct vision from all sides (Fig. 2). With this wide exposure in a cavity of such amplitude, the technical manipulation of cutting anterior and posterior apron flaps of peritoneum for suspension of the





Fig 5, left Total gastrectomy for carcinoma of the linitis plastica type, together with a very large spleen with attached vasa brevia. This spleen was of such size as to interfere with total removal of the stomach. This is one of the early cases in which the omentum was not removed.

Fig 6 Total gastrectomy for carcinoma of the linitis plastica type, together with splenectomy, indicated by the arrow.

anastomosed jejunum, as devised and advocated by one of us<sup>1</sup> in a technical article on total gastrectomy, together with the introduction of the anastomosing sutures, is made surprisingly easy.

#### CONCLUSIONS

The occasional advantage of combining splenectomy with total gastrectomy is advocated when in this operation oozing, particularly from the splenic veins in the hilum of the spleen, occurs.

<sup>1</sup>Labey, F. H. Complete removal of the stomach for malignancy with a report of five surgically successful cases. *Surg. Gynec. & Obst.*, 1918, 67: 212-223.

during the course of the operation, when with malignancy on the greater curvature it is desirable to undertake a wider removal than could be accomplished with the spleen remaining, and particularly when an enlarged spleen so hampers exposure at the gastro esophageal junction that safe anastomotic sutures cannot be inserted under good direct vision.

Its addition as a technical step in total gastrectomy so adds to the ease with which the operation may be performed that it lessens rather than adds to the risk of the operation.

# MUCOCELE OF THE APPENDIX AND PSEUDOMYXOMA PERITONEI

## A Clinical Review and Experimental Study, with Case Report

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THE term "mucocoele of the appendix" was first introduced by Feré (1876) to apply to the enlargements of the appendix containing mucous or pseudomucous material. According to Masson and Hamrick (1930), Virchow was the first to describe this condition in 1863, but Weaver (1937) credits Rokitsky with having described the pathology in 1842. Secondary peritoneal deposits resulting from rupture of mucocoele of the appendix were first designated as "pseudomyxoma peritonei" by Fraenkel (1901), although Werth (1884) had previously used the same term to apply to the secondary peritoneal deposits or growths resulting from rupture of certain ovarian cysts. Our interest in this subject was stimulated by a clinical case, a report of which is given below. It is our purpose, following this case report, to review our clinical knowledge of mucocoele of the appendix and pseudomyxoma peritonei, and to report the results of animal experimentation carried out in an attempt to reproduce these conditions.

### CASE REPORTS

Mr. D. P., aged 44 years, was first seen by one of us (M.G.) on November 6, 1939, with a chief complaint of general abdominal pain of one day's duration. There was some nausea but no vomiting. The bowels had not moved since the onset of illness. The temperature was normal and the pulse 80. Examination of the abdomen revealed moderate tenderness in the lower right quadrant, over McBurney's point and closer to the midline. There was marked muscle guard making it difficult to palpate any masses. The patient stated that he had had a similar attack about 1 year previously from which he had recovered under conservative management.

Laboratory findings were as follows: red blood cells, 5,300,000; hemoglobin 102 per cent; white blood cells, 12,400; segmented cells, 62 per cent; staff cells, 8 per cent; lymphocytes, 19 per cent; eosinophils, 3 per cent; mononuclears, 8 per cent. Urinalysis showed specific gravity, 1028; albumen, negative; sugar, negative. Microscopic examination showed 1 or 2 red blood cells and 30 to 35 white blood cells per high-power field.

A diagnosis of acute or subacute recurrent appendicitis was made and operation was advised. This was refused at first but consented to the following day.

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Operation was performed November 7, 1939, by Dr. Grodinsky. Under gas-ether anesthesia, the abdomen was opened through a McBurney incision. There was considerable clear free fluid in the peritoneal cavity. A large mass was encountered posteromedial to the cecum, and adherent to the cecum and small bowel. After careful separation by sharp and blunt dissection, this mass proved to be a greatly enlarged appendix. The mesoappendix and base of the appendix were ligated with chromic No. 2 catgut and the appendix was removed. The stump was carbolized but not inverted. A limited exploration revealed no further pathology in the abdomen. The abdominal wall was closed in layers without drainage.

Pathological report by Dr. Rubnitz: The appendix was egg-shaped, measuring 8.5 centimeters in length and 5 centimeters in diameter (Fig. 1). The surface was red, injected, and somewhat roughened in the areas where adhesive bands had been separated during removal. The lumen was filled with thick, jelly-like material typical of mucus. This material gave a reduction test for mucin and stained red with mucicarmine. The wall was made up of fibromuscular tissue infiltrated with leucocytes (mostly lymphocytes). The mucosa was totally atrophied, no epithelial cells being demonstrable (Figs. 2 and 3). Pathological diagnosis: mucocoele of the appendix.

The patient made an uneventful recovery and, when last seen, October, 1940, was in good health.

### CLINICAL REVIEW

Very little appeared in the literature on this subject until 1909, when cases were reported by Neumann in Europe and Kelly in this country. Interest again lagged until 1915, when Phemister described the clinical and pathological picture in detail, and attempted to reproduce the condition in dogs. Between 1915 and 1930, there appeared scattered reports by Castle (1915), Nash (1919), Davison (1922), Milliken and Poindexter (1925), and Topping (1928). In 1930, Masson and Hamrick reviewed the literature and described 6 cases. Following this, numerous articles appeared both in this country and abroad. Among them were the papers of Vorhaus (1930), Birkenfeld (1931), Squires (1931), Kemkes (1932), Mayo and Fauster (1932), Hentz (1932), Lifvendahl and Ries (1932), Bell (1935), Abdanski (1936), Wilmoth (1936), Jones and Carmody (1936), Jackson (1936), Olson (1936), Sarff (1936), Dannreuther (1936), Weaver (1937), Morgan (1937), Waugh and Findley (1937), Bittmann (1939), Dordick

(1939), Latimer (1940), and Woodruff and McDonald (1940).

**Incidence.** Kelly (1909), quoting Stengel, gave an incidence of 0.3 per cent for mucoceles, in 9,108 autopsies. This agrees quite closely with Castle's (1915) figure of 0.2 per cent. Mayo and Fauser (1932) reported 76 mucoceles in 31,200 appendectomies, an incidence of 0.24 per cent. On the other hand, Dannreuther (1936) reported an incidence of only 0.1 per cent in 8,457 appendectomies, and Weaver (1937) of 0.11 per cent in 6,225 appendectomies. According to Jones and Carmody (1936), the total number of cases of mucocele of the appendix reported up to that time was approximately 400. D'Aunoy and Fine (1934) estimated the total number of reported cases of pseudomyxoma peritonei of appendiceal origin to be 90. Phemister (1915) stated that mucocele is associated with normal involution of the appendix in patients between the ages of 35 and 50. The average age was found by Masson and Hamrick (1930) to be 57 years (6 cases) and by Mayo and Fauser (1932) 42½ years (70 cases). Dannreuther (1936) reported mucocele most common in patients past middle age. Most authors have found a slightly greater incidence in females than in males.

**Etiology.** As has been stated, Phemister (1915) thought the condition was due to normal involution of the appendix and the commonly associated inflammation. Milliken and Poindexter (1925) described three steps in the formation of mucocele: (1) secretion of mucin into the crypts, (2) failure of reabsorption, (3) the conversion of mucin into pseudomucin. Vorhaus (1930) described a preliminary step in the formation—stenosis, although he reported a case diagnosed before operation by ingestion of barium and examination by x-ray. A similar case was reported by Lifvendahl and Ries in 1932. This would indicate that complete or permanent obstruction at the base is not necessary and that infection may enter the lumen of the appendix. Perhaps it is the amount and character of the infection which determines whether a relatively sterile mucocele or an infected, gangrenous appendix results from partial or complete obstruction at the base. Wangenstein and his associates (1937, 1939) have repeatedly demonstrated the production of acute appendicitis by obstruction of appendices not previously irrigated. Mayo and Fauser (1932), Jones and Carmody (1936), Dannreuther (1936) and Jackson (1936) described the essential steps in the formation of mucocele and pseudomyxoma peritonei as obstruction, absence of gross infection, secretion faster than absorption, distention,

formation of diverticula and rupture with the formation of secondary pseudomyxoma peritonei. Our observations would seem to confirm this view.

**Pathology.** The size of mucoceles of the appendix varies greatly, from that of a normal appendix to that of a man's head. The shape may be globular, egg-shaped, conical, or sausage-like, depending on the location of the obstruction in relation to the base of the appendix (Neumann, 1909, Nash, 1919; Jones and Carmody, 1936; Jackson, 1936; Weaver, 1937).

The nature of the wall is likewise quite variable. In general, however, the earlier stages reveal a hyperplastic, secretory mucosa with cuboidal or columnar goblet cells, considerable round cell infiltration of the submucosa and hypertrophy of the muscularis. With increasing distention of the lumen by accumulated secretion, the mucosa becomes gradually atrophic and, in the larger specimens, epithelial cells are entirely absent. Likewise in the later stages, the rest of the wall becomes thinned out with loss of muscle fibers and replacement by connective tissue. With the thinning of the wall and the increase of internal pressure, diverticula may form on the mesenteric or antimesenteric borders. Finally, rupture of the wall of the diverticula or of the appendix proper may occur, with extrusion of the contents of the lumen into the general peritoneal cavity and formation of secondary growths or deposits, pseudomyxoma peritonei. The secondary growths or deposits are usually incapsulated by walls of fibrous tissue with varying degree of inflammatory, cellular infiltration (Phemister, 1916, Nash, 1919, Milliken and Poindexter, 1925; Mayo and Fauser, 1932, Abdanski, 1936, Jones and Carmody, 1936, Jackson, 1936, Olson, 1936, Sarff, 1936, Dannreuther, 1936, Morgan, 1937).

The contents of mucoceles vary according to the stage, degree of inspissation, and amount of cellular reaction. The earlier formations contain a somewhat thin, clear or slightly turbid, sticky fluid. This becomes thicker and more gelatinous with the reabsorption of water. Where considerable leucocytic reaction has occurred, the contents become whitish, putty-like or cheesy in consistency, resembling caseous or necrotic material. Many authors make a distinction between true mucin and pseudomucin on the basis of staining reaction (mucicarmin) or the reduction tests (Hammarsten, 1904, Lewis, 1914; Phemister, 1915, Nash, 1919, Milliken and Poindexter, 1925, Masson and Hamrick, 1930, Vorhaus, 1930, Birkenfeld, 1931, Hentz, 1932, Wilmoth, 1936 and Morgan, 1937). However, all gradations of staining reactions occur and reduction tests may

be obtained with true mucin. It seems therefore an unnecessary and valueless distinction, and the term pseudomucin had best be abandoned with the realization that a variety of chemical compounds exists in the substance commonly known as mucin.

Some mucoceles contain small, globular, semi-transparent bodies the size of a millet or sago seed (1 to 10 mm. in diameter) within the diffuse mucous contents. These are probably localized areas of inspissation occurring in regular formation (Milliken and Poindexter, 1925; Hentz, 1932).

That the contents of a mucocele may be actually bactericidal has been suggested by Lifvendahl and Ries (1932). The fact that our material, obtained from the contents of mucoceles and pseudomyxomata peritonei, could be kept for long periods without preservatives and did not show evidence of decomposition would seem to support this contention. This may help explain the relative sterility of the contents of mucoceles and the failure of appendicitis and gangrene to occur.

The secondary peritoneal deposits or transplants following rupture of mucoceles of the appendix vary in their contents in the same way as the original mucoceles, depending upon the same factors. However, due to the greater inflammatory reaction, leucocytic infiltration is more common in these secondary deposits, the contents of which are therefore usually opaque and white in color.

**Complications.** The commonest complication, or rather sequela, of mucocele of the appendix, according to most authors (Phemister, 1915; Jackson, 1936; Dannreuther, 1936; Morgan, 1937, etc.) is pseudomyxoma peritonei. As stated previously, this name was first applied to the daughter peritoneal lesions resulting from rupture of mucocele of the appendix by Fraenkel (1901), although the term had been previously applied by Werth (1884) to similar peritoneal lesions resulting from rupture of certain ovarian cysts. Thus, this condition may result from either mucocele of the appendix or ovarian cyst in the female, but from mucocele of the appendix alone in the male.

Intestinal obstruction from pressure of the enlarging mucocele of the appendix or from intussusception due to the presence of the mucocele has been reported in several cases (Morgan, 1937). Associated carcinoma of the appendix has likewise been reported. It has been suggested that this malignancy may cause the obstruction of the lumen which allows the accumulation of mucus and the production of mucocele, or that the mucocele

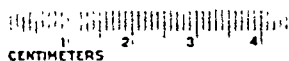


Fig. 1. Photograph of mucocele of the appendix in clinical case (D.P.). Part of wall removed to show mucous contents. Photograph taken after fixation, some shrinking having occurred.

may bring about stimulation of the epithelium and secondary malignant change (Vaugh and Findley, 1937). Diverticula of mucoceles of the appendix are common. Dordick (1939) reported a case of mucocele of the appendix with three solid diverticula filled with neuromatous overgrowth and one cystic diverticulum filled with mucus similar to that within the appendix.

**Clinical picture.** The symptoms of mucocele of the appendix are rather vague and indefinite (Phemister, 1915; Vorhaus, 1930; Jones and Carmody, 1936; Jackson, 1936). There is usually pain in the lower right quadrant of the abdomen, but this is not apt to be severe or well localized. The initial epigastric or paraumbilical pain of acute appendicitis is often absent. There may be slight nausea, usually without vomiting. Fever and leucocytosis are also apt to be absent. Constipation may or may not be present. Muscular rigidity is not present unless there is marked associated inflammatory reaction. Sometimes the symptoms are those of intestinal obstruction due to pressure of the mucocele on adjacent loops of bowel or to intussusception. Quite often the mucocele is large enough to be palpated through the abdominal wall and this facilitates the diagnosis. If the obstruction to the lumen of the appendix is incomplete or the lumen has reopened, the appendix may be visualized by the ingestion of barium and by x-ray examination, thus further aiding in the diagnosis (Vorhaus, 1930; Lifvendahl and Ries, 1932). However, the diagnosis is seldom made preoperatively, and operation is



Fig 2, left Photomicrograph of section through wall of mucocoele of appendix (D P), showing atrophy of mucosa and replacement fibrosis (Hematoxylin and eosin)  $\times 30$

Fig 3 Photomicrograph of inner part of same section Note the cellular infiltration, and the absence of epithelial cells in the mucosa (Hematoxylin and eosin)  $\times 435$



Fig 4, left Photomicrograph of section through wall of normal rabbit appendix, showing thin seromuscular layer and very thick submucous or lymphoid layer with cone-shaped lymphoid follicles arranged at right angles to long axis of appendix (Mallory's C T stain)  $\times 30$

Fig 5 Photomicrograph of section through wall of mucocoele of appendix in rabbit 8, showing relative and absolute increase in thickness of seromuscular layer and marked decrease in thickness of lymphoid layer with change in axis of lymphoid follicles (Hematoxylin and eosin)  $\times 30$

usually performed for appendicitis which most closely resembles this condition

**Treatment and prognosis** The treatment of mucocoele of the appendix consists essentially of

appendectomy. As long as the lesion is confined to the appendix and no leakage has resulted into the general peritoneal cavity, complete recovery is the rule. If leakage has occurred and daughter

lesions are present scattered through the peritoneal cavity, the prognosis is much more serious. Due to their multiplicity and indefinite outlines, it is physically impossible to remove all such secondary deposits or transplants surgically. There is evidence that at times the secondary lesions will disappear following the removal of the primary lesion by appendectomy. However, the secondary lesions often take on malignant characteristics and continue to grow after the removal of the appendix. This has led to the view that two types of secondary pseudomyxomatous growths may result: the one, a benign, passive deposit of the mucous contents from the appendix which may reabsorb after the removal of the primary lesion; the other, a transplant of epithelial cells from the appendix to the general peritoneal surfaces where they take on malignant characteristics. Woodruff and McDonald (1940) believe that malignant, pseudomyxomatous growths, secondary to mucocoele of the appendix, occur only as the result of the transplantation of epithelial cells from previously existing malignancy in the appendix. However, the possibility of change in the serosal cells themselves by stimulation from the appendiceal contents must also be kept in mind. X-ray treatment for pseudomyxoma peritonei is recommended by some authors (Masson and Hamrick, 1930), but its value has not been proved and is difficult to evaluate as long as the secondary lesions may disappear spontaneously after removal of the appendix. More often the pseudomyxoma assumes malignant characteristics and results fatally.

#### ANIMAL EXPERIMENTATION

Naeslund (Masson and Hamrick, 1930) produced mucocoele of the appendix and pseudomyxoma peritonei in rabbits by ligating the base of the appendix. Similar results were obtained by Antoine (1935). Phemister (1915) attempted to reproduce the condition in 7 dogs by dividing the caecal appendage at the base and closing both ends without disturbing the blood supply. All but 1 dog developed gangrene and peritonitis. In the one exception, the lumen had become re-established and the cecal appendage returned to normal. Phemister believed that the failure was due to the too sudden obstruction with the shutting off of the intrinsic blood supply by distention.

In a very exhaustive and conclusive series of experiments, Wangenstein and his associates (1937, 1939) studied the problem of production of appendicitis in dogs and other animals by various means of obstruction to the lumen of the appendix. They showed that obstruction plus infection,



Fig. 6. Photograph of mucocoele of appendix and secondary implant in rabbit S. Note that part of the contents of the appendix had been lost before this photograph was taken.

almost invariably produced appendicitis and gangrene, whereas infection alone did not. On the other hand, increase in the intraluminal pressure, even in relatively noninfected (washed) appendices, resulted in shutting off the intrinsic blood supply and in gangrene of the organ. Obstruction in the washed cecal appendages of dogs was found to be usually well tolerated, resulting either in normal appendages or occasionally in mucocoele.

Wells (1937) was able to produce mucocoele in rabbits by ligation of the base of the appendix without ligation of the vessels. When trauma to the mucosa was added to this procedure, acute appendicitis resulted. Wangenstein was not able to confirm the results of Wells in regard to the effect of trauma to the mucosa. Wells did not state whether the appendices had been irrigated before ligation, a procedure which, we found, has an important influence upon the results.

In casting about for a laboratory animal suitable for experimental production of mucocoele, we came to the conclusion that, of the common laboratory animals, the rabbit possesses an appendix most closely resembling that of the human in structure and function. This opinion agrees with that of Wangenstein and his associates (1940) who studied the appendix from a standpoint of comparative anatomy and came to the conclusion that only the rabbit and anthropoid ape possess appendices resembling the human, morphologically and physiologically.



Fig 7, left Photomicrograph of section through wall of secondary implant, rabbit 8, showing general arrangement of the entire wall and zone of necrosis near inner surface (DeLafield's hematoxylin and eosin—azure II)  $\times 30$

Fig 8 Photomicrograph of part of same section under higher magnification, showing giant cells, large mononuclear cells, histiocytes and isolated epithelium like cells (DeLafield's hematoxylin and eosin—azure II)  $\times 435$

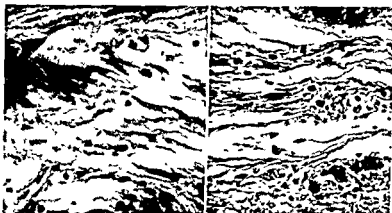


Fig 9, left Photomicrograph of part of section through thicker part of wall of secondary implant, rabbit 8, showing young connective tissue of myxomatous character (Mallory's C T stain)  $\times 435$

Fig 10 Photomicrograph of part of section through wall of neck of secondary implant, rabbit 8, showing more mature connective tissue and increased vascularity (Mallory's C T stain)  $\times 435$

*The normal rabbit appendix* In the rabbits used in our experiments, weighing between 5 and 6 pounds, this structure is larger than in the human, averaging about 10 centimeters in length and 1 to 1.5 centimeters in diameter. There is a double blood supply, from the appendiceal vessels

and from the vessels of the adjacent loop of jejunum, both of which lie in a common mesentery. The wall of the appendix is much thinner than in the human, particularly the seromuscular layer which makes up only about 4 per cent of the wall. The submucosa or middle layer, on the

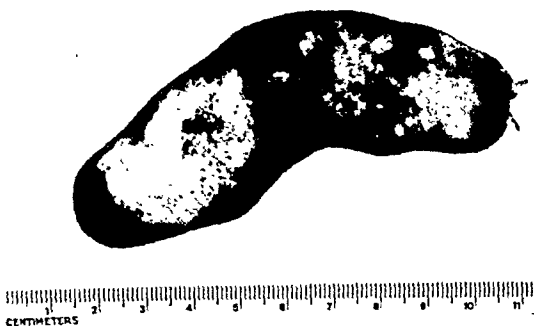


Fig. 11. Photograph of mucocoele of appendix produced by ligation in rabbit 16.

other hand, is much thicker than in the human and forms the bulk of the appendiceal wall, comprising about 72 per cent of the total thickness. This layer consists of elongated, cone-shaped follicles of lymphoid tissue, arranged at right angles to the long axis of the appendix and separated from each other by fibrous trabeculae extending from the seromuscular layer to the mucosa. The inner or mucous layer makes up about 24 per cent of the total wall. The epithelial cells of the mucosa, for the most part, closely resemble the mucin producing cells in the human appendix and are normally filled with their mucinous secretion (Fig. 4). In both the rabbit and human, the appendix is chiefly an organ of secretion rather than of absorption.

**Material and methods.** Twenty-six rabbits were used in the ligation and injection experiments. In the ligation experiments, each animal was operated upon at least twice: the first operation consisting of ligation of the appendix and the second of exploration of the peritoneal cavity from 2 to 8 weeks later. Some animals were operated upon three or four times. Ligation was usually done about 2 centimeters distal to the base of the appendix, to facilitate later removal of the appendix with the original ligature included. The appendiceal vessels were not included in the ligature. Silk or flat umbilical tape was used for ligating, with equal success in most cases. In our experience, the tightness of the closure was a very important part of the procedure. We felt that some of our failures to produce mucocoele were due to the incomplete closure of the lumen. In the first two experiments, the appendices were ligated without preliminary irrigation of the lumina. Both animals died of gangrenous appendicitis and peritonitis. In subsequent experiments, we preceded the ligations by irrigation of the lumina with 60 to 80 cubic centi-



Fig. 12. Photograph of mucocoele of appendix and secondary implants in mesentery of small gut, with segment of latter, rabbit 12.

meters of normal salt solution, using a syringe and needle as suggested by the work of Wangenstein and his associates (1937). This procedure insured relatively clean lumina before ligation and resulted in reduction in the mortality rate practically to zero, except when complicating factors were present.

In the injection experiments, the animals were injected intraperitoneally with material taken from the contents of mucocoeles or from the contents (and walls) of pseudomyxomatous lesions produced in other rabbits. When the material was too thick to go through a needle, it was first emulsified and diluted with sterile normal salt solution. In a few instances, the material was passed through a Seitz filter, and the filtrate and residue (or original substance) were injected into separate animals. An ordinary Luer syringe and No. 20-22 gauge needle, about 1.5 inches long, were used for the injections.

**Results of ligation.** By the technique described mucocoeles, varying in size and stage according to the lapse of time between operations, were produced almost at will (10 out of 12 animals) (Figs. 6, 11 and 12). In addition, when sufficient time was allowed to elapse between ligation and the secondary exploration, rupture of or extension through the walls of mucocoeles with the production of secondary deposits or implants, pseudomyxomata peritonei, took place in several animals (6 of 10 animals that developed mucocoeles) (Figs. 6 and 12). The following protocol of the experimental work on rabbit 8 is typical and is reproduced as an example of the findings in several (6) of these animals.

**Rabbit 8.** First operation, March 21, 1940. Sodium pentobarbital intravenously, supplemented by ether, was used for the anesthetic. Through a midline incision, the appen-





Fig 13, left Photograph of secondary lesions in rabbit 18, resulting from the intraperitoneal injection of the contents of the mucocele in rabbit 12

Fig 14 Photomicrograph of part of section through larger lesion shown in Fig 13, showing myxomatous character of tissue (Mallory's C T stain)  $\times 445$

dix was irrigated with 60 cubic centimeters of normal salt solution and ligated near base with umbilical tape, tight enough to obstruct the lumen. Closure was made in layers.

A second operation was performed April 29, 1940. The same anesthetic was used. Through a midline incision the peritoneal cavity was opened, and several mucus like deposits were seen on the surface of the omentum. The appendix was distended, red, and adherent to adjacent loops of intestine. It was about 8 centimeters long, 3 centimeters in diameter at the base and 2 centimeters in diameter at

the tip (Fig 6). There was a pin head size opening near the base through which clear mucus could be forced by pressure. A large bulb-shaped, cystic tumor, about 7 by 6 centimeters in size was found between the great omentum and the mesentery of the small intestine (Fig 6). There were several large retroperitoneal lymph nodes. The liver and spleen were normal except for a pin head size nodule in the capsule of the liver.

Microscopic sections of the appendix showed the sero-muscular coat to be markedly thickened while the middle or lymphoid layer was proportionally thinner, the lymphoid follicles assuming an oval shape, parallel with the long axis of the appendix. The inner or mucous layer was of about the same thickness as in the normal appendix. The glands and the mucin producing epithelial cells appeared quite active and normal. The three coats were of about equal thickness, in contrast to the normal condition, and the total thickness of the appendiceal wall was much less than that of the normal rabbit appendix (Fig 5).

The large, bulb-shaped secondary tumor contained a thick, white, viscid fluid, consisting of mucus and degenerated inflammatory cells. Sections were taken through three parts of its wall. One section (Figs 7 and 8), through the thinner part of the wall, showed the latter to consist of mature connective tissue infiltrated with lymphocytic cells especially toward the inner surface, where there were many degenerated red blood cells and leucocytes. Just external to this surface, the cellular infiltration consisted of large mononuclear cells, some histiocytes, occasional foreign body giant cells, and isolated epithelium like cells. A section (Fig 9) through the thicker part of the wall showed the latter to consist of very young connective tissue, some of it distinctly myxomatous in character. The cellular infiltration was more marked, the cells being mainly large mononuclears (plasma cells) with a liberal sprinkling of eosinophils. Near the inner surface, there were many partially degenerated red blood cells and leucocytes. Finally, a section (Fig 10) through the neck of the tumor again showed a more mature type of connective tissue in the wall, which was very vascular.

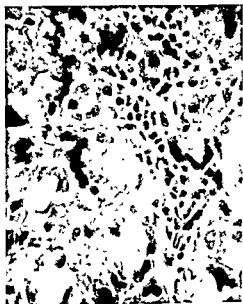


Fig 15 Photomicrograph of part of section through secondary lesion in rabbit 17, resulting from intraperitoneal injection of emulsion of secondary deposits found in rabbit 12. Note the apparent incompletely formed gland tubules (Mallory's C T stain)  $\times 535$

**Results of intraperitoneal injections.** Since secondary deposits resulted from spontaneous rupture of mucoceles of the appendix, it was considered feasible to attempt the production of

pseudomyxomata peritonei by intraperitoneal injections of the contents of mucocèles and of secondary deposits into other rabbits. Because of excessively hot weather during the later period of the experimental work, 6 animals were lost from heat exhaustion. Nine other animals were used in this group of experiments; 7 injected with the contents of mucocèles and 2 with an emulsion of the contents, or of the contents and wall, of secondary deposits. Of the 7 animals injected with the contents of the mucocèles, 5 were injected with the whole contents or residue and 2 with the filtrate after passing the contents through a Seitz filter. Neither of the latter developed lesions, but 3 out of the 5 injected with the whole contents or residue showed typical pseudomyxomatous deposits in the peritoneal cavity (Figs. 13 and 14). The 2 animals, injected with an emulsion of the contents or of the contents and wall of secondary deposits, both developed pseudomyxomatous lesions of their own (Fig. 15).

*Other types of experiments.* A few variations in technique and findings may be noted. In one rabbit, the appendix was severed at the base between ligatures, the blood supply having been preserved and the lumen irrigated, as in the other animals. However, the animal died in one week of acute appendicitis and general peritonitis. In another, a seton thread was introduced into a mucocèle of the appendix at the second operation purposely to permit leakage. However, at the next operation, this opening had sealed over and no secondary deposits had resulted. In still another animal, a gross opening was made in the appendix. This resulted in peritonitis and death in a few days. The contents of one mucocèle were injected intravenously into another rabbit without any demonstrable result. One rabbit, which had developed secondary deposits after the intraperitoneal injection of the contents from the mucocèle of another rabbit, showed a disappearance of the lesions upon secondary exploration several weeks later. A second injection was attempted, but the animal died of heat exhaustion. This experiment would indicate the production of an immunity reaction and recalls the tendency of some pseudomyxomatous lesions in the human to disappear after removal of the primary lesion.

*Contents of mucocèles and secondary deposits of experimental animals.* The material recovered from the mucocèles and secondary deposits varied in consistency from that of a clear, thin, viscid fluid to that of a thick, transparent or translucent, gelatin-like substance, depending upon the degree of inspissation which in turn seemed to depend upon the time elapsed since ligation. When there

was much inflammatory reaction with leucocytic infiltration, the material was more opaque and white in color, resembling cream or putty according to the amount of fluid present. This was especially true of the secondary deposits, only a few of which were transparent in character. Chemically, the material was mucous in character, as shown by reduction tests and mucicarmine staining reactions. Bacteriologically, the contents of the mucocèles showed many small gram-negative (colon) and large gram-positive bacilli on smears and cultures. Hanging-drop preparations contained large sausage or balloon shaped bodies in which double, spherical objects were inclosed, like two peas in a pod. This picture could not be demonstrated in stained preparations. The contents of the secondary pseudomyxomatous lesions showed no organisms on direct smears and were sterile on cultures.

*Microscopic picture.* The histopathology of the appendices and secondary deposits in the experimental animals presents many interesting observations and opens up several new problems, the details of which will be considered in a later paper. In the smaller and younger specimens of mucocèles, the epithelial cells show little change but, in the older and larger specimens, the epithelial cells may become compressed and flattened by the pressure of the contents within the lumina, and eventually undergo atrophy and disappear. The most striking change, however, is in the middle layer. The normally thick layer of lymphoid tissue becomes much thinned out and the axis of the lymph follicles becomes parallel to the long axis of the appendix, due to pressure from within the lumen. The normally thin seromuscular layer may be thickened at first due to inflammatory reaction and fibrous tissue increase, but it later becomes thinned out by stretching. All the layers contain inflammatory cells, chiefly leucocytes with many eosinophils (Fig. 5).

The secondary deposits consist of an outer wall of young or more mature connective tissue, at times distinctly myxomatous in character. The central portions are usually necrotic, containing many inflammatory cells in various stages of disintegration. Toward the periphery of the necrotic central zone, these cells are better preserved and consist of many eosinophils intermingled with large mononuclear cells, occasional larger histiocytes and giant cells (Figs. 7 to 10, 14, and 15).

*Summary of animal experiments.* Mucocèles of the appendix were produced in rabbits in a large proportion of attempts, by a definite technique. When sufficient time elapsed, secondary deposits in the same animals often occurred by sponta-

neous rupture of, or extension through, the walls of the mucoceles. Secondary deposits were also produced in animals by the intraperitoneal injection of the contents of mucoceles or of emulsions of the contents and walls of the secondary deposits of other animals. However, the filtrates of these materials, after passing through a Seitz filter, were unable to produce lesions when injected intraperitoneally, indicating that the responsible substance was not filterable and was possibly cellular. The question is opened up as to whether the secondary deposits are the result of actual transplantation of viable cells, or the result of stimulation or irritation of cells *in situ*. This interesting speculation on cellular pathology merits further study.

#### SUMMARY AND CONCLUSIONS

1. The literature on mucocele of the appendix and pseudomyxoma peritonei has been reviewed with particular reference to the clinical and pathological pictures. A personal case is described. The treatment, as recommended, consists of removal of the mucocele of the appendix and of radiotherapy of the pseudomyxomatous lesions when present.

2. In a series of animal experiments upon 26 rabbits, each operated upon 2 or more times, mucocele of the appendix and pseudomyxoma peritonei were frequently produced by a definite technique.

3. The most striking etiological factor in the production of mucocele is the obstruction at or near the base of the appendix, with a relatively clean but not necessarily bacteriologically sterile lumen.

4. A similar obstruction with a grossly infected lumen leads to acute appendicitis and gangrene.

5. Pseudomyxoma peritonei results from rupture of, or extension through, the mucocele wall and widespread dissemination of the mucous contents along peritoneal surfaces.

6. The question is raised as to whether the pseudomyxomatous lesions are the result of actual transplantation of epithelial cells from the appendiceal mucosa or the result of specific irritation of the serosal cells by the mucous contents. Further work will be necessary to answer this question.

7. In some of our experiments, there is evidence of the development of an immunity reaction, with the disappearance of secondary pseudomyxomatous lesions following the removal of the primary mucocele. Similar results have been reported in some clinical cases. In most of the clinical cases reported, however, the pseudomyx-

omatous lesions assumed malignant characteristics and led to a fatal outcome.

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# THE LATERAL APPROACH TO A DIVERTICULUM OF THE ESOPHAGUS

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THE most usual of the diverticula of the esophagus is the one which appears in the midline of the posterior wall just below the pharynx, and for this reason it is sometimes called a pharyngoesophageal diverticulum. It is a pulsion or hernial sac and protrudes through a weak triangular area left by the fibers of the constrictor muscle as they pass around the back of the esophagus. It starts as a small pit or depression of the mucosa which gradually enlarges and, after it has extended beyond the wall of the esophagus, it impinges on the curving anterolateral wall of the vertebrae and, aided by gravity, begins to extend downward. Because the esophagus in this region is usually to the left of the midline the diverticulum is found most frequently on the left side of the neck.

The symptoms are exactly what one might expect in a growth of this nature, and they increase in severity as the sac increases in size. At first there is a little hesitation in the customary effortless act of swallowing; gradually this becomes more pronounced, and later actual difficulty may develop. Gurgling while drinking may be quite embarrassing to the patient and at times splashing can be heard. Food which has been swallowed some hours previously and thought to be well on its way may suddenly reappear in the patient's mouth when he lies down or leans over. As the size of the sac increases the weight of its contents gradually pulls it beneath the pharynx so that the stoma of the sac comes to lie directly in line with the superior or proximal end of the esophagus. Food then passes directly into the diverticulum and that portion of the esophagus which lies next to the diverticulum is compressed and this interferes with the easy passage of the food into the stomach. When this stage is reached actual starvation may develop, and, if the diverticulum is large enough to press on the trachea, difficulty in breathing may be present.

Palliative treatment is not very successful. The patient learns early that by pressing on the side of his neck he can help himself swallow, or that he can empty a sac which has become uncomfortably filled. The condition, however, is slowly

progressive and surgery is the only form of treatment which holds out any hope of relief.

## ANATOMY

A surprising amount of anatomy is concealed within the small circle of the neck. Beneath the skin and platysma the sternomastoid is our main landmark. Medial to the anterior border of this muscle lies the carotid sheath with its contents, the carotid artery, the jugular vein, and the vagus nerve. Slightly posterior but almost in the same plane lie the so called ribbon muscles, the sternohyoid and the sternothyroid. In the midline and posterior to these muscles lies the trachea with the isthmus of the thyroid lying over the anterior surface and the lobes lateral to it. Posterior to the trachea is the esophagus and the diverticulum with which we are now concerned appears on its posterior surface and thus lies just anterior to the

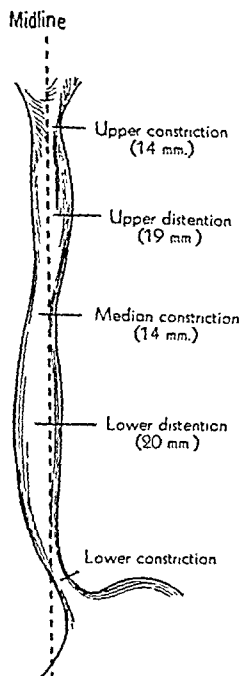


Fig. 1. Outline of the esophagus, showing the curvature to the left in the neck.

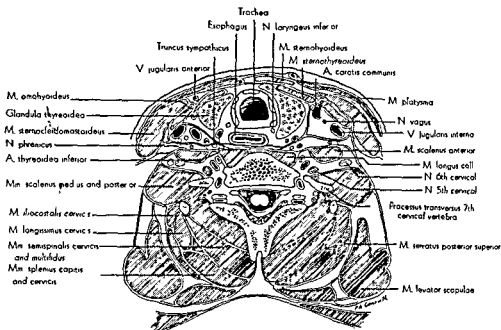


Fig. 2. Cross section of the neck at the level of the seventh cervical vertebra showing the fascias and structures involved in both routes to the diverticulum (Modified from Eycleshymer and Schoemaker)

cervical vertebrae. Several other structures should be mentioned, namely the blood supply to the thyroid, the recurrent nerve, and the omohyoid muscle which runs diagonally across the neck from the hyoid to the shoulder.

#### OPERATION

*The anterior approach.* The incision is made along the anterior border of the sternomastoid muscle. The sternomastoid with the carotid sheath is retracted laterally, while the ribbon muscles and the thyroid gland are retracted medially. Usually the omohyoid muscle is divided. The recurrent nerve is identified so as to avoid any possible damage to it. And finally the esophagus is identified and the diverticulum found and dissected free. These, very briefly, are the steps taken in the operation commonly used in the excision of a pulsion diverticulum of the cervical portion of the esophagus.

#### POSTERIOR APPROACH

Several months ago a patient came in complaining of dysphagia, regurgitation of food, gurgling upon drinking, and dyspnea. A diagnosis of esophageal diverticulum was made and confirmed by the x-ray. During the examination there came to mind a fact frequently demon-

strated in the anatomy laboratory, namely that abscesses in or near the cervical vertebrae almost invariably follow along the prevertebral fascia and point at the side of the neck posterior to the sternomastoid muscle. Continuing this thought it began to look as though it might be more logical, instead of the more usual complicated approach in front of the sternomastoid, to make an incision posterior to this muscle and use the prevertebral fascia as a guide to the region between the esophagus and the vertebral column. Before an operation was attempted, however, an anatomical comparison of the two approaches was made on the cadaver. Four dissections were done, two anterior and two posterior to the sternomastoid muscle. Cross sections of the neck were also examined and the conclusion was reached that the posterior approach was not only simpler and quicker but was considerably safer than was the anterior approach.

This posterior approach is based on planes of cleavage as determined by the fascial planes of the neck. The deep fascia as it is followed from behind the neck toward the front is found to divide at the posterior border of the sternomastoid to enclose this muscle, and then it passes on to enclose the omohyoid and the ribbon muscles in front. Near the posterior border of the

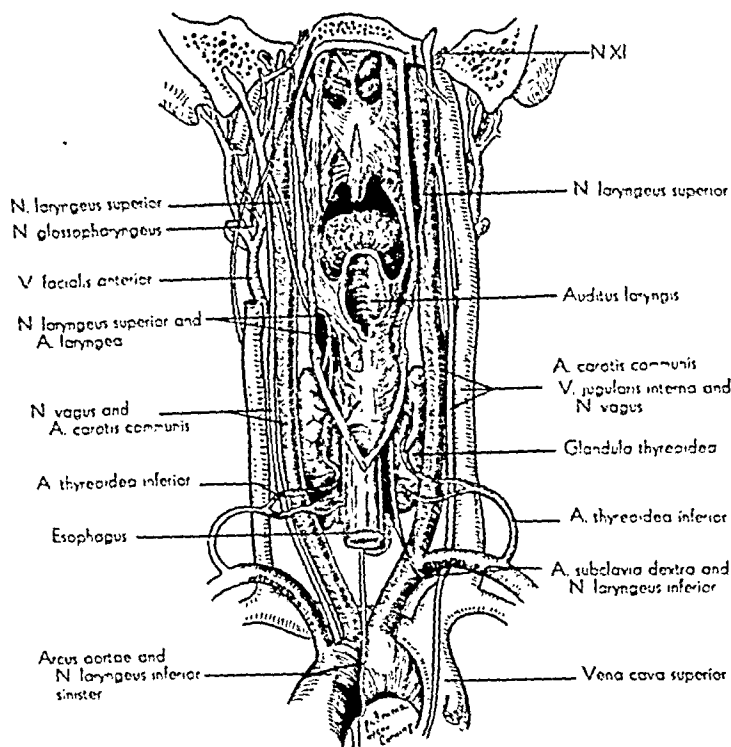


Fig. 3. The structures which lie anterior to the prevertebral fascia, viewed from behind.

sternomastoid, the inner sheath of this fascia again divides to form the prevertebral fascia which passes directly medialward between the esophagus and the cervical vertebrae. Behind the prevertebral fascia lie the vertebrae, the vertebral muscles and the nerves of the brachial plexus, which, however, emerge from behind the scalenus anterior and are thus amply protected. The phrenic is the only nerve running down the anterior surface of the scalenus. Anterior to the prevertebral fascia are the soft vital structures of the neck, the esophagus, the trachea, the thyroid with its blood supply, the recurrent nerve, and the carotid sheath which is a triangular space, the lateral wall of which is formed by the medial portion of the sheath of the sternomastoid, the medial wall is formed by the pretracheal fascia which passes medialward anterior to the trachea enveloping the thyroid as it does so, while the posterior wall is formed by the prevertebral fascia.

An incision made along the posterior border of the sternomastoid and deepened along the posterior surface of the prevertebral fascia will lead directly to the region behind the esophagus, and

the operator will have the soft vital structures of the neck safely in front of this incision instead of having to dissect down between them. The posterior border of the sternomastoid is grasped by forceps and retracted gently forward and medially carrying with it the carotid sheath. Posterior to this muscle the prevertebral fascia can easily be felt and by blunt forceps and finger dissection it is followed medially. As the midline of the neck is reached the fascia will be found to become quite friable so no difficulty should be experienced in breaking through it to the esophagus. The diverticulum can then be found and dealt with as conditions dictate. If the diverticulum is large and has descended quite low in the neck or even into the thorax the lower end of this wound will be quite near the midline, thus affording ample room for dissection. This is a distinct advantage since with the anterior approach the lower part of the incision becomes constricted with the approach of the sternomastoid and carotid sheath toward the midline. There is so much more room with this incision that one may get right down behind the subclavian, and

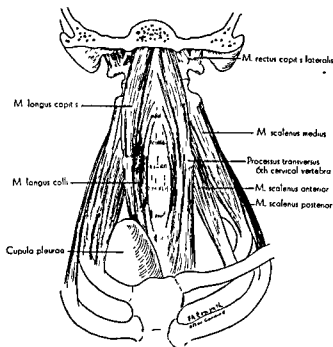


Fig 4 Structures lying posterior to the prevertebral fascia

it would seem to be an excellent site for the exteriorization of the esophagus in cancer of the distal end.

The disadvantages are few. The distance from the posterior border of the sternomastoid to the

midline of the neck may be slightly greater than it is from the anterior border, but the directness of the approach, the freedom from dealing with vital structures, and particularly the roominess at the lower end of the incision more than make up for it. There should be no apprehension about disturbing the phrenic nerve as it lies snugly against the scalenus muscle and is not attached to the prevertebral fascia. The spinal accessory nerve may be cut if the upper end of the incision is carried too high, but this can usually be avoided. The branches of the superficial cervical nerves as they emerge from the posterior border of the sternomastoid can also be avoided, and probably no more of them will be severed with this incision than with the other.

Throughout this paper the terms "posterior approach" and "anterior approach" have been used because of the reference to the sternomastoid. The "posterior approach" lies well to the lateral side of the neck and the dissection leads directly medially and for this reason the term "lateral approach" might be more descriptive.

A rather complete search of the literature as far back as 1895 has failed to reveal the use of anything but the usual anterior incision. If this lateral incision has been used before it has either

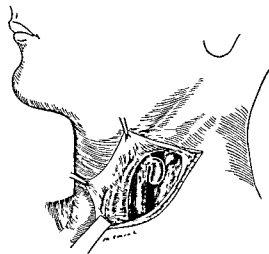


Fig 5 View of the diverticulum through the posterior or lateral incision.

not been reported or has been missed by the author.

This lateral incision appears to be an excellent approach to the cervical portion of the esophagus and I believe warrants the consideration of the men who might use it.

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# A STUDY OF THE MOTILITY OF THE INTACT UTERUS AT TERM

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CONTRARY to the general trend of reports during the last two decades, two recent papers have presented direct evidence for the hormonal nature of the oxytocic principle of the hypophysis. Haterius and Ferguson (1938) demonstrated powerful and prolonged augmentation of uterine activity in rabbits shortly after parturition as a result of electrical stimulation of the pituitary stalk. The response was elicited after all probable nerve paths from the hypothalamus to the uterus were cut, but was not obtained after destruction of the pituitary body. Chang, Lim, Lu, Wang, and Wang (1938) reported increased oxytocic activity in the blood of nonpregnant bitches as a result of electrical stimulation of the central ends of the vagus nerves. Their blood and extracts were tested on isolated guinea pig uteri.

In his recent monograph, Reynolds (1939) has criticized the conclusions of Haterius and Ferguson on the grounds that the augmentation of uterine activity might have been due to the small and transient rises in blood pressure which occurred at the same time. In conversation Dr. Reynolds has offered another criticism, namely, that certain devious nerve paths from the hypothalamus to the uterus might have escaped section. He suggested that crushing the neck, leaving the carotid arteries and jugular veins as the only connection between the head and the trunk, would be a more convincing way to rule out nervous transmission.

The experiments presented in Section I of this paper were designed to test the objections to the experiments and conclusions of Haterius and Ferguson and to extend the observations to another species, the cat. The results support unequivocal-

ly the conclusions that direct stimulation of the pituitary stalk can liberate an oxytocic hormone. Section II contains certain observations on the motor reactions of rabbit and cat uteri near the time of parturition which suggest mechanisms which may control the secretion of the oxytocic hormone in the intact animal and the movements of the uterus during parturition.

## SECTION I

*Methods.* In all experiments cats or rabbits 2 to 48 hours after parturition have been used. Uterine contractions were usually recorded by a Cushny myograph (1906) attached at two points on one horn about an inch apart along the longitudinal axis. Another method of recording often used simultaneously with the Cushny myograph was cannulation of the horn, either through an incision in the upper part of the vaginal wall and then through the cervix or through an incision in the uterine wall itself. The uterus was then distended with saline and the fluctuations in pressure recorded by a stiff tambour. The degree of activity recorded by this method depended somewhat on the degree of distention, but the changes in activity in response to various stimuli were very similar to those recorded by the myograph.

The animals were anesthetized with a mixture of 1 per cent chloralose in 10 per cent urethane, given in the amount of 4 cubic centimeters per kilogram intravenously to the rabbits and intraperitoneally to the cats. This was supplemented by ether for the operative procedures, which consisted of tracheotomy, isolation of the carotid arteries, external jugular veins, and vagus nerve trunks, and trephining of the skull. A femoral vein and artery were cannulated for injections and the recording of blood pressure respectively. The apparatus for recording uterine contractions was



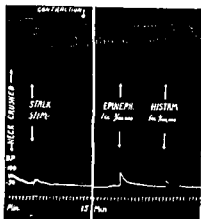


Fig 1 The upper tracing shows uterine contractions in a rabbit 24 hours post partum recorded by the Cushny myograph. The lower record is of blood pressure in the femoral artery. The powerful and prolonged contractions of the uterus elicited by electrical stimulation to the pituitary stalk after the neck was crushed contrast strongly with the effects of epinephrine and histamine injected intravenously.

introduced through an incision in the midline or in the flank. The head was then mounted in a special headholder. This device orients the head by fixing three points, the two external auditory meatuses and the necks of the central incisors, or, in the case of cats, the maxillary bone just above the central incisors. Bipolar electrodes are carried on a rack and pinion adjustment (giving movement in three dimensions), and attached to the frame of the headholder. The electrodes are sighted on the midline over the trephine hole and set at a mark on the anteroposterior scale which has been found to lie directly over the middle of the pituitary fossa. The electrodes may then at the appropriate time be inserted to a depth indicated on another scale and which has been found to bring the tips of the electrodes about 1 millimeter above the roof of the pituitary fossa. It has been found empirically that the electrodes are in proper position when stimulation produces a bilateral flutter of the eyelids and twitching of the whiskers. The electrodes were made of No. 22 gauge nichrome wire, lacquered to the tips and separated by only 0.1 millimeter. They were excellent for applying localized stimuli with the inductorium, but for destroying the pituitary body by direct current the lesions produced were too localized. Wires separated by about 0.5 millimeter were better. As in previous work, the vibrator of the inductorium was weighted to diminish the frequency of the breaks to about 8 per second.

For crushing the neck obstetrical cranioclastic forceps were used. The jaws were placed in position and, at the proper time, screwed tightly together leaving only the carotid arteries, jugular veins, and a flap of skin as the sole functional connections between the head and the trunk. Autopsies showed that the spinal cord was completely severed by dislocated vertebrae at the level of the third or fourth cervical segment. Artificial respiration was started after the neck was crushed. The blood pressure, after an initial rise of variable size, gradually fell to shock levels. In most of the later experiments the fall in blood pressure was delayed by continuous infusion of saline, or saline with 6 per cent gelatine, with or without the aid of ephedrine (about 2 mgm.) injected intravenously. This dose of ephedrine had no effect on the movements of the uterus and often by itself was sufficient to maintain the blood pressure at a level high enough to sustain active uterine movements, namely 50 to 70 millimeters of mercury.

**Procedure.** Typical experiments were conducted as follows. After the preparatory operations the uterine contractions were recorded for  $\frac{1}{2}$  to 1 hour. The contractions were usually quite infrequent, provided the uterine muscle was only slightly stretched by the recording apparatus.

In some experiments certain drugs were injected during this period to compare their effects with those of stalk stimulation and of pitocin or pituitrin. In other experiments the drugs were injected after the effects of pitocin and stimulation had been elicited. The drugs used were epinephrine, acetylcholine, and histamine since it was conceivable that the electrical stimuli in the brain stem might release one or more of these substances. It may be said here that none of these substances produced effects at all comparable to the effects of stimulation or of pitocin, as Figures 1 and 2 illustrate. The complex effects of epinephrine are discussed in Section II. Acetylcholine in doses sufficient to lower the blood pressure by 40 to 50 millimeters had scarcely any effect on uterine motility, somewhat larger doses gave complex effects like those of epinephrine.

In some experiments the initial control period was followed by an injection of pitocin, in others by a stimulation of the stalk. In others again the crushing of the neck was done immediately. After the crushing, a further period of 15 to 25 minutes was allowed to elapse while the effects of this procedure on the uterine movements was observed. As a rule the crushing of the neck by itself had little effect on the uterine contraction and never evoked a sustained increase in activity.

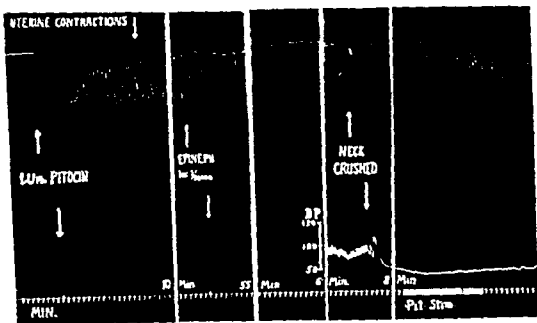


Fig. 2. Uterine contractions induced by pitocin in a cat 8 hours post partum before the crushing of the neck are shown for comparison with the contractions induced by stimulation of the pituitary stalk after. A common effect of epinephrine is also illustrated.

**Observations.** In consecutive experiments on 6 rabbits and 5 cats, stimulation of the pituitary stalk after the neck was crushed, in every case, produced a change in uterine contractions similar to that produced by pitocin injected intravenously. The most characteristic features of the response in both species were the increased frequency of contractions and the long duration of the increased activity, a matter of 1 or 2 hours. In both cats and rabbits the response to stimulation of the stalk was about equal to the effect of 0.5 unit of pitocin.

In 3 cases after a further period of an hour to an hour and a half after the neck was crushed, a second stimulus gave a similar, but not quite so great, response.

In 1 other case in which a second stimulus was attempted, no response was obtained, probably because of the poor condition of the uterus after a long period of low blood pressure. In this case the injection of 1.0 unit of pitocin a few minutes later also failed to stimulate the uterus.

Associated with the uterine response to stimulation of the stalk there was usually a small rise in blood pressure which raised the question as to whether a pressor hormone was liberated as well as an oxytocic one. In this connection it should be noted: (a) that one of the illustrations (Fig. 2) shows only a very slight rise in blood pressure which follows the onset of the uterine contractions; (b) that in all tracings as the uterine activity subsides from the tetanic level each separate contraction is associated with a rise in blood pressure; (c) that closer analysis of the tracings shows that these periodic rises of blood pressure follow, rather than precede, the uterine contractions, which fact suggests that the blood pressure rise is a mechanical consequence of the uterine contrac-

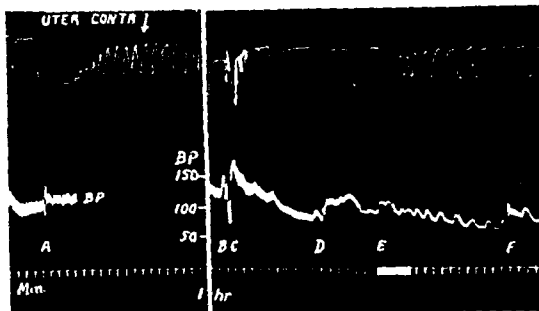


Fig. 3. Cat 24 hours post partum. At A, 1 unit of pitocin was injected intravenously. At B, the neck was crushed, and at C the vagi were divided. At D, 20 cubic centimeters of saline was injected intravenously with practically no effect on uterine motility, although the rise in blood pressure was greater than that produced by pituitary stimulation at E. Rises in blood pressure with each uterine contraction are well illustrated. At F, another 20 cubic centimeters of saline was injected without effect on the uterine motility. The fall in blood pressure was minimized by an injection of 2 milligrams of ephedrine before the neck was crushed.

tions, as noted by Franklin (1935). In 1 experiment stimulation of the stalk was followed by an injection of 1 unit of pituitrin and then of 1 unit of pitocin. The pituitrin gave a larger rise in blood pressure than did stimulation of the stalk, but actually diminished uterine motility due presumably to its vasoconstrictor action in the uterus. The pitocin produced simultaneously with uterine contraction a small rise in blood pressure about equal to that obtained on stimulation of the stalk. These observations suggest that the hormone liberated by stimulation of the stalk in these animals has little pressor action and resembles pitocin more than whole pituitrin.

**Evaluation.** The rises in blood pressure accompanying the uterine response were suspected by Reynolds of causing the response. Although Figure 2 by itself is sufficient to rule out the possibility, other considerations pointing to the same conclusion should be mentioned. A rise in blood pressure is illustrated in Figure 3 at D, which was produced by the slow injection of 20 cubic centimeters of normal saline, while the blood pressure was falling after the neck was crushed. Although the rise in blood pressure thus produced was greater than the rise produced shortly after by the stimulation of the stalk, no augmentation of uterine activity resulted from the saline injection.

Another simple consideration discounting the possibility that the rise in blood pressure caused the uterine response is the fact that the uterus was relatively inactive when the blood pressure was high, before the crushing of the neck, but

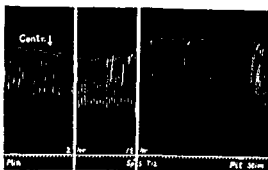


Fig 4. This tracing illustrates the gradual increase in uterine activity in a rabbit about 24 hours post partum, during 7 hours of recording without interference, together with the decline in activity following spinal transection. The integrity of the uterus and pituitary gland were demonstrated at the end by electrical stimulation of the pituitary stalk. The decline in uterine activity is attributed to interruption of afferent impulses from the lower cord maintaining secretion of oxytocic hormone.

greatly augmented after stimulation of the stalk, although the blood pressure was lower than before the crushing of the neck.

Many observations have indicated that a very low blood pressure can depress the activity of the postpartum uterus. Rises in blood pressures may restore activity suppressed in this way, but they have not been observed to initiate activity.

#### SECTION II

The experiments in this section had the object of identifying characteristic reactions of the uterus near the time of parturition. With typical reactions identified, it became possible to assess the importance of secretion of oxytocic hormone and of purely nervous factors in each reaction. The results have provided new viewpoints on the mechanism and onset of parturition.

**Methods.** Rabbits, 8 to 48 hours after parturition, were used unless otherwise stated. The anesthetics, operative procedures, and methods of recording uterine motility were usually those described in Section I. For visual observations of the uterus the abdominal cavity was exposed by a special retractor and protected from drying by a sheet of cellophane. The stimuli most frequently tried were dilatation of the vagina, the cervix, and the uterine horn. The vagina was dilated by inflating a finger cot on the end of a glass tube inserted through the os vaginae, the cervix by a glass dilator inserted through an incision in the vagina. The uterine horn was usually dilated with saline through a cannula inserted through an incision in the wall of the horn. In later experi-

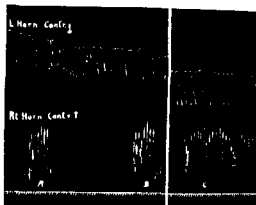


Fig 5. The contractions of the left uterine horn of a rabbit are recorded by a Cushny myograph. The contractions of the right are recorded by a tambour only when the horn is distended with saline as at A, B, and C. The distention of the right increases the movements of the left horn before destruction of the hypophysis, A and B, but not after, C.

ments a finger cot was used. In no case did the size of any of the dilators exceed that of a fetus at full term.

**Observations.** When the abdomen was opened 8 to 24 hours after parturition the uterus was nearly always large, flabby, and inactive. On exposure to air it contracted but even after attaching the recording apparatus the contractions were usually feeble and infrequent. During the subsequent half hour or less, the contractions gradually increased in strength and frequency until a level of activity was reached which was maintained fairly uniformly for as long as observations were continued without interference: a matter of 4 hours in 1 case and of 2 hours or more in many other experiments.

The slowly mounting activity of the first half hour was attributed at first to the elimination of the ether used in the operation or of the basal anesthetic. It soon became evident, however, that readministration of ether until all reflexes were abolished had no immediate depressing effect on the uterine contractions (confirming Cushny, 1906), nor had the administration of more chloralose and urethane. If deep anesthesia were maintained for a quarter of an hour or more, a slow decline in uterine activity developed. These observations suggested that the effect of the anesthetic might not be directly on the uterus or on purely nervous reflexes, but on reflex maintenance of tonic secretion of oxytocic hormone, or perhaps on a tonic secretion of oxytocin dependent not on afferent nerve impulses but on "spontane-

ous" nervous activity in the brain stem. That oxytocic hormone is important for the maintenance of a high level of activity has been abundantly indicated by the fact that destruction of the pituitary body by electrolytic burns has consistently led, both in these experiments and in those of Haterius and Ferguson (1938), to a gradual decrease in the uterine activity in a matter of an hour or so.

To test whether tonic secretion was reflexly maintained by impulses from the pelvic region, the spinal cord was transected in 7 experiments at the twelfth thoracic segment while the uterine activity was high. In every case the uterine activity gradually decreased and within an hour and a half the contractions were very infrequent (Fig. 4). The decline in activity resembled the decline after an injection of pitocin. In 3 experiments the functional integrity of the uterus was demonstrated at the end of this period by an injection of pitocin (0.2 to 0.5 unit). In the 4 others the integrity of both the uterus and the hypophysis was demonstrated by electrical stimulation of the pituitary stalk. Each time a vigorous response of the uterus was obtained. It appears then that afferent impulses from the lumbosacral cord are important in maintaining a tonic secretion of oxytocic hormone.

*Uterine dilatation.* The main source of the afferent impulses maintaining secretion of hormone under the conditions of these experiments appears to be the stretching of the uterine horn by the recording apparatus. In 3 experiments, relaxation of the tension on the uterus by bringing the arms of the Cushny recorder closer together resulted in a gradual decrease in the frequency of the contractions. Stretching the horn again brought a gradual decrease in frequency. No changes in frequency were obtained by changing the stretch on the uterus after the pituitary had been destroyed, even before the activity of the uterus had declined appreciably. The contractions merely became less and less frequent.

It may be contended that in these experiments changes in stretch altered merely the irritability and contractility of the stretched muscle. If this possibility is not thought to be adequately excluded by the ineffectiveness of stretching after destruction of the pituitary, it appears to be by experiments in which stretching one horn brought about gradual increase in frequency of the other. In 6 experiments one horn was dilated with saline, while the contractions of the other were recorded with the Cushny myograph. In 3 cases in which the preliminary activity was low, definite augmentation of activity of the unstretched horn was

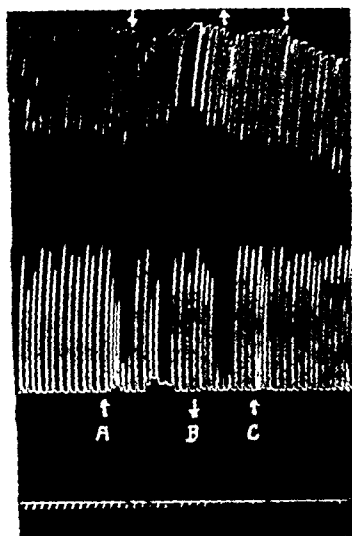


Fig. 6. Simultaneous record of the contractions of the right and left uterine horns in a rabbit are shown. The top record is by the Cushny myograph, the lower by a tambour connected to the left horn which is filled with saline. At A a vaginal dilator was inserted and inflated. At B the dilator was slowly pulled out through the os, producing another response. Both are qualitatively similar to the effect of 1 cubic centimeter of epinephrine 1:100,000 injected intravenously at C. Time intervals 1 minute.

observed. The effect was abolished by destruction of the pituitary (Fig. 5). In 3 other cases no definite augmentation was observed, but in all of these the preliminary activity was very great, due perhaps to the stretch imposed by the cannula in the uterine horn. This factor was not appreciated when the experiments were done. The slow augmentation and slow decline of activity on stretching should be distinguished clearly from an immediate effect of great dilatation of the uterine horn on its own contractions, with no immediate effect on the contractions of the other horn. This effect was an immediate increase in frequency with considerable irregularity, as if contractions were starting in various parts of the horn and interfering with propagated synchronous contractions.

*Vaginal dilatation.* In each of 12 experiments, dilatation of the vagina produced a definite change in the uterine activity. The nature of the change depended somewhat on the circumstances and sometimes appeared to have two components, producing some mutual interference. The most prominent component may be called the "immediate biphasic reaction." This reaction was elicited in pure form (a) in the more deeply anesthetized animals, (b) after destruction of the

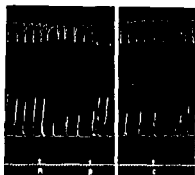


Fig 7. A record of contractions from both uterine horns in a cat is shown. At A a vaginal dilator is inflated, at B deflated. At C, 1 cubic centimeter of epinephrine 1:100,000 is injected intravenously.

pituitary, (c) after cord section at the twelfth thoracic segment; hence, it is probably reflex, involving not more than the lumbosacral cord. It consists of an immediate increase in frequency lasting for 3 to 5 minutes, followed by decrease in frequency (below the control frequency) lasting 3 to 10 minutes. The changes in amplitude are not characteristic or reproducible even in the same animal (Fig. 6). The amplitude may increase or decrease in either phase. This mixed response resembles the characteristic response of the parturient uterus of both cat and rabbit to epinephrine. An atypical but instructive example is illustrated in Figure 8 in which a cat uterus responds to both vaginal dilatation and epinephrine with a biphasic response in which, however, the phase of decreased frequency (and amplitude) comes first. From the foregoing evidence it may be postulated for the time being that the immediate biphasic response is a reflex, involving the adrenergic innervation of the uterus. A similar reaction is often observed, not only on inflation of the vaginal dilator, but also on the insertion and removal of the dilator through the os vaginae.

The second component of the response to vaginal dilatation may be called the "slow augmentation reaction." In lightly anesthetized intact animals this reaction is sometimes superimposed on the immediate biphasic reaction, with the result that the uterine contractions are somewhat irregular, but tend to increase in frequency and amplitude. The augmentation outlasts the dilatation and subsides slowly, like the effect of stretching the horn. It has not been obtained after destruction of the hypophysis or after section of the spinal cord. In any case it is not obtained as consistently by stretching the vagina as by stretching the uterine horn.

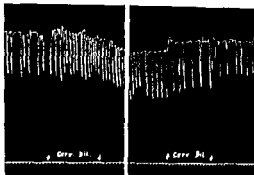


Fig 8. The effect of dilation of the cervix before destruction of the hypophysis is shown in the first section, and its lack of effect after destruction of the hypophysis in the second.

A third effect of vaginal dilatation does not strictly concern the uterus but is of interest. It is a "bearing down" contraction of the abdominal muscles. It is feeble or absent in deep anesthesia and disappears after section of the cord at the twelfth thoracic segment. No attempt has been made as yet to determine the pathways of this interesting reflex. The adequate stimulus appears to be dilatation of the vagina or rectum. Stretching the cervix does not produce it.

A fourth effect of vaginal dilatation observed visually in 2 cases is a powerful contraction of the cervical region. This contraction quickly involves the upper end of the vagina and is propagated downward as an expulsive peristaltic wave.

**Cervical dilatation.** Stretching the cervix in 8 of 10 experiments has produced a uterine reaction of the slowly augmenting, slowly subsiding type. In each case the reaction was abolished by destruction of the pituitary or by section of the cord (Fig. 8). The 2 failures were earlier experiments in which the initial activity of the uterus was great. In 2 of the 8 experiments there has been a suggestion of an immediate biphasic component, but this might have been due to the manipulation of the vagina during the introduction of the cervical dilator.

The experiments to date give the impression that the reaction suggestive of release of oxytocic hormone is elicited most effectively by dilatation of the cervix, almost as effectively by the stretching of the horn, but only occasionally and feebly by the stretching of the vagina.

**Afferent vagal stimulation.** The claim of Lum and his co-workers that stimulation of the central ends of the vagus nerve in the neck, liberates pressor hormone from the pituitary prompted a trial of this type of stimulation in the rabbit. In 3

of 5 experiments definite augmentation of uterine activity of the slowly augmenting, slowly subsiding, type was obtained. It is uncertain whether these results indicate a physiological afferent pathway through the vagi or merely represent an irradiation of intense activity in the brain stem.

*Evaluation.* In a study of the effects of epinephrine on excised rabbit uteri near the time of parturition, Bonnycastle and Ferguson (1940) stress the variation in the response of different parts of the uterus to epinephrine. They conclude that epinephrine is predominantly motor to the circular muscle at the cervical end of the uterus, and to a lesser degree to the circular muscle of the rest of the horn. The longitudinal muscle of the horn was less frequently stimulated than the longitudinal muscle at the cervical end, and indeed is often inhibited. The functional effect of epinephrine was deduced to be antiexpulsive: (a) by tending to make the cervical end the pacemaker for contractions of longitudinal muscle, (b) by promoting contraction of the cervix and other circular muscles, (c) by inhibiting synchronous contractions of the longitudinal muscle which must be the most powerful agent of expulsion. They contrast the nonexpulsive effects of the powerful contractions produced by epinephrine given to rabbits at term with the immediate expulsive effect of small injections of pitocin. On the basis of these experiments, it is suggested that the component of the response to dilatation of the vagina, which resembles that of epinephrine, is a mechanism for co-ordinating the emptying of the uterine horns. Dilatation of the vagina by the entry of a fetus would cause reflexly a contraction of the cervix and probably other effects on the horn, resembling those of epinephrine. Thus the emptying of the horns would be delayed until the vagina had been emptied.

#### EVALUATION

The observations of this paper suggest some additions to current hypotheses concerning the onset and mechanism of parturition, at least in the rabbit. Stretching the uterus appears to maintain a tonic secretion of oxytocin. Whether this is true throughout pregnancy remains to be determined. In any case the effect would not be important because of the insensitivity of the uterus to oxytocin until the end of gestation (Knaus, 1926). As the sensitivity to oxytocin increased, contractions forcing the fetus against the cervix would increase and would be most likely to stretch the cervical region at a time sympathetic activity tending to contract the cervical region was at a low level. Stretching the cervix would augment the secretion

of oxytocin and provide added impetus to expulsion, since the cervix itself is relatively insensitive to oxytocin (Newton, 1937; Bonnycastle and Ferguson, 1940). Expulsion of the fetus into the vagina might liberate even more oxytocin, but its main effect would be to cause contraction of the cervix and, by this and its other actions, to delay the expulsion of more fetuses till the vagina was emptied. The known factors are sufficient to explain the evacuation of several fetuses from a horn in orderly succession, starting with the lowest one. If oxytocin initiates contractions in the longitudinal muscle of all the ampullae, as it appears to from inspection, it is in the lowest ampulla that contractions, propagated toward the vagina, will be least likely to meet contractions propagated in the opposite direction, because of the insensitivity of the cervical region to oxytocin. In all the higher ampullae expulsive contractions are likely to be opposed by contractions starting below. In fact, the interampullary nodes are likely to be kept in fairly constant activity by contractions reaching them from both above and below, and might be expected to act like sphincters in high tone. With the lowest ampulla empty, and the stimulus of stretch thus removed, retrograde contractions opposing the expulsive contractions of the ampulla above would cease, or at least become less frequent, and allow it to empty in its turn.

Certain phenomena of parturition in the human may be interpreted rather plausibly in view of the findings of this paper. It is generally observed that labor pains increase in frequency and strength as the cervix dilates. They reach their maximum in the second stage when the cervix is fully dilated. It is plausible to suppose that in the human, as in the rabbit, stretching the cervix may augment the secretion of oxytocin. This may explain why a dilating bag or rimming of the cervix is so effective for inducing labor. Rupture of the membranes, forcing the presenting part against the cervix, may achieve the same result more slowly. Involuntary "bearing down" in the human is characteristic of the second stage of labor when the fetus is stretching the vagina; thus the adequate stimulus for bearing down may be the same in the human as in the rabbit.

The effect of epinephrine on uterine contractions in the human seems to be the same as in cats and rabbits. The records of Bourne and Burn (1930) taken during parturition show that 0.3 milligram of epinephrine given intravenously produces an initial augmentation of contraction followed by inhibition, resulting in a 10 minute pause in the midst of regular 5 minute pains, which may be utilized in obstetrics to perform versions.

## SUMMARY

In Section I further evidence is presented that electrical stimulation of the pituitary stalk in rabbits and also in cats shortly after parturition liberates an oxytocic hormone.

In Section II the effects of stretching the uterine horn, cervix, and vagina and certain other stimuli on the uterine activity are analyzed. The evidence indicates that dilatation of the cervix augments uterine motility by reflexly liberating oxytocin. Dilatation of the horn, remote from the cervix, does so too, but less consistently. Dilatation of the vagina only occasionally releases oxytocin but consistently produces a complex change in uterine activity similar to the effects of epinephrine. It is suggested that

vaginal dilatation reflexly delays the emptying of the horns until the vagina is emptied.

Aspects of parturition in rabbits and humans are discussed.

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# A STUDY OF THE BACTERIOLOGY OF THE CERVIX DURING PREGNANCY AND ITS RELATION TO PUERPERAL MORBIDITY

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A STUDY of the medical literature of the past 40 years reveals many articles dealing with the incidence of pathogenic organisms in the cervix and vagina of women during pregnancy and their importance as a contributing cause in increasing puerperal morbidity and mortality. It is now well known that the genital tracts of women harbor a variety of organisms which morphologically and culturally are identical with bacteria which do initiate pathological changes, although the incidence of such organisms varies greatly in reports of different observers. Most obstetricians agree that autoinfection from the cervix and vagina is a negligible factor in the causation of puerperal sepsis. Some indeed insist that it never occurs and that puerperal infection is always due to introduction of pathogenic organisms from without. However, most men of wide experience can recall patients who developed severe and fatal puerperal infection in which the most painstaking investigation revealed no possibility of exogenous source.

In 1898, after bacteriological examination of the vaginal secretion in 92 pregnant women, Williams (15) concluded that the usual pyogenic cocci were not present so that death from puerperal infection is always due to infection from without. He did admit the possibility, in very rare instances, that the vagina may contain bacteria which give rise to sapremia and putrefactive endometritis by autoinfection.

Bumm and Sigwart (1904) studied 103 women and, using solid culture media, were able to isolate aerobic streptococci in three-fourths of them prepartum, intrapartum, or postpartum. They believed that with better culture media (bouillon) streptococci would be found in the vaginal secretion of all pregnant women. They presumed that virulence was promoted by the streptococcus working in symbiosis with other organisms present and by change in local conditions making the locus ideal for proliferation and elaboration of toxin. Their study of the puerperia of these

women led to the conclusion that there is no definite relationship between streptococci found prepartum and puerperal morbidity.

Fromme (1910) from his studies concluded that it was impossible to estimate the virulence of a specific strain of streptococci because of variation in individual resistance. He did not believe that the ordinary streptococcus strains which are found postpartum can gain in virulence nor that saprophytic streptococci found prepartum can result in puerperal infection.

Medalia and Walton (1912) studied 103 cases antepartum and postpartum and concluded: (1) hemolytic or nonhemolytic streptococci causing morbidity are not necessarily of exogenous origin; (2) autoinfection plays an equal rôle with exogenous infection as to frequency of sepsis but not as to its severity.

Fricke (1914) studied the vaginal secretion in 50 women awaiting delivery at the Hopkins Clinic using a variety of culture media. Streptococci were isolated from the vulva in 14 per cent, from the vagina in 8 per cent. In 47 prepartum women examined at home the percentages were 75 and 55 per cent, respectively. He attributed the 7 times greater incidence in homes to less personal cleanliness. One-third of the organisms were hemolytic.

Kantor and Pilot (1924) studied bacteriologically 96 prepartum women of various parity, with clinical follow-up in the puerperium of 67. They concluded that hemolytic streptococci are rarely present in the normal vagina and when present are not very virulent.

Eeles (1925) examined 31 primiparae and 39 multiparae and found the *Bacillus coli* in 4, *Staphylococcus albus* in 34, diphtheroid bacillus in 35, *Staphylococcus aureus* in 1. The streptococcus was found in 5 multiparae and in 6 primiparae. Only 1 was hemolytic.

White and Armstrong (1928) indicated that previous studies of the bacteriology of the cervix and vagina during pregnancy were inconclusive because no attempt was made to designate the type of streptococcus. In a study of 153 cases

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(141 primigravidae, 12 multiparae) they found aerobic streptococci 36 times, anaerobic 55 times. Only 34 of the combined groups exhibited hemolytic properties. No cases of true sepsis occurred in the women whose prepartum cultures had given positive cultures of *Streptococcus hemolyticus*. Of the 127 patients whose cultures were negative for *Streptococcus hemolyticus* there were 5 morbid puerperia and 1 typical streptococcal septicemia. In each of these latter, the *Streptococcus pyogenes* was cultured from the cervix and in the last one from the blood stream. Their results seemed to indicate definitely an exogenous origin for infection in puerperal sepsis.

Bryce (1928) studied cervical cultures in cases of fever following childbirth or abortion. He concluded that the presence of a number of organisms in the genital tract is usually associated with a mild type of disease. The isolation of one strain only may or may not be significant. The presence in pure culture of the *Streptococcus pyogenes* or the gonococcus appears to indicate the accession of invasive power which is associated with virulence. The work did not indicate whether the association of mild disease with the absence of streptococci means that these organisms have never been present either as pre-existing or introduced inhabitants or whether the resistance of the host has been sufficient to inhibit the development of virulence on their part.

The *Annals of the Pickett-Thompson Research Laboratory* (1929) record the following organisms as having been isolated from the female genital tract: *Streptococcus pyogenes puerperalis*, facultative anaerobic diplococcus, *Staphylococcus albus*, bacteria of coli group, *Bacillus pseudotetanus*, *Bacillus aerogenes capsulatus*, *Streptococcus viridans*, *Streptococcus mitior*, *Streptococcus fecalis*, *Staphylococcus aureus*, diphtheroids, yeasts, molds, pneumococcus, *Micrococcus tetragenus*, *Streptococcus mitis*, *Streptococcus infrequens*, *Streptococcus equinus*, *Bacillus welchii*, *Döderlein's bacillus*, *enterococcus*, *Bacillus subtilis*, and *Bacillus mycoides*.

DeLee (1929) stated that mild cases of autoinfection may occur occasionally, fatal cases are exceedingly rare.

Williams (16, 1930) concluded that while bacteriological research affords a certain amount of evidence in favor of the theoretical possibility of autoinfection, clinical observation speaks against it. Accordingly the occurrence of serious streptococcal infection should always be regarded as evidence of external infection.

Logan (1931) isolated streptococci 70 times in a study of 200 prepartum cases (35 per cent)

*Bacillus coli* was isolated from 10 of the same group (5 per cent). None of the streptococci were hemolytic. Only 5 per cent of these patients had postpartum morbidity of the British Medical Association standard. There was an increase in puerperal morbidity incident to operative interference. Contrasting the puerperia of those with and without positive prepartum cultures led the author to conclude that the presence of a non-hemolytic streptococcus in the vagina during pregnancy has no apparent bearing on the production of puerperal sepsis.

Watson (4, 1933) states that the general consensus is that autoinfection is not common. It has been considered a possibility that autoinfection from the vagina or cervix may be the explanation of those cases of infection occurring in women on whom no internal examination has been made and who have had a spontaneous and unaided delivery.

Harris and Brown (1926) have shown that the fourchette and fossa navicularis contain a rich bacterial flora which may be carried into the female genital tract when vaginal and cervical cultures are taken. Adair et al. (1933) confirmed this conclusion.

This study was undertaken in an attempt to answer the following questions:

1. What is the incidence of pathogenic organisms in the cervix of pregnant women since previous publications give a wide divergence of results.
2. What is the relationship between cervical erosion and previous mild chronic cervicitis as contributing factors to the presence of these organisms?
3. What effect does parity have on this incidence?
4. Is there a seasonal variation in the presence of pathogenic organisms?
5. Has the stage of gestation an effect on the incidence?
6. Does the evidence support the occurrence of autoinfection?

Cultures were taken from the cervixes of 275 consecutive patients admitted to the maternity clinic at the Pittsburgh Hospital. To eliminate the personal factor, all cultures were taken by two of the authors (E. A. C. and D. L. O'L.). The following technique was used: The labia were separated and the vestibule cleansed carefully with cotton pledgets soaked in 4 per cent boric acid solution, a sterile bivalve speculum was introduced, opened, and passed into the vagina so that the cervix was exposed without touching it; 2 cultures were taken, the cervix was then cleansed and inspected.

TABLE I.—RESULTS OBTAINED IN CULTURES MADE IN 275 PATIENTS

	Aerobic	Anaerobic
Total no. cultures made	275	167
Organisms isolated		
<i>Staphylococcus albus</i> .....	182	84
<i>Staphylococcus aureus</i> .....		1
<i>Staphylococcus citreus</i> .....	1	
<i>Staphylococcus hemolyticus</i> .....	2	
<i>Micrococcus flavus</i> .....	2	
<i>Pneumococcus</i> .....	4	1
<i>Micrococcus pharyngis siccus</i> .....	1	
<i>Micrococcus catarrhalis</i> .....	3	
<i>Micrococcus tetragenus</i> .....	4	2
Large gram-coccus unidentified.....	1	
Diphtheroid bacillus.....	15	13
Friedlaender's bacillus.....	2	1
<i>Bacillus lactis aerogenes</i> .....	1	
<i>Bacillus proteus</i> .....		2
<i>Bacillus subtilis</i> .....	20	12
<i>Bacillus xerosis</i> .....	1	
<i>Bacillus coli communis</i> .....	4	5
<i>Bacillus coli communior</i> .....	4	2
<i>Bacillus pseudodysentericus</i> .....	1	
<i>Bacillus fecalis alcaligenes</i> .....	2	1
<i>Bacillus smegmatis</i> .....	3	2
Gram positive bacillus unidentified.....	1	2
Gram negative bacillus unidentified.....	1	
Gram positive spore bearing bacillus.....	2	
<i>Bacillus mesentericus</i> .....	1	
<i>Leptothrix</i> .....	6	28
<i>Streptothrix</i> .....		1
<i>Nocardia</i> .....		2
Yeast cells and bacilli.....	15	10
<i>Streptococcus pyogenes hemolyticus</i> .....	3	
<i>Streptococcus hemolyticus</i> unidentified.....	3	2
<i>Streptococcus hemolyticus anginosus</i> .....	1	
<i>Streptococcus hemolyticus equinus</i> .....	1	
<i>Streptococcus mitis viridans</i> .....	11	12
<i>Streptococcus salivarius</i> .....	1	1
<i>Streptococcus fecalis</i> .....	2	1
<i>Streptococcus viridans</i> unidentified.....	5	2

TABLE II.—EFFECT OF EROSION AND CERVICITIS ON PRESENCE OF PATHOGENIC ORGANISMS IN CERVIX

Erosion	Yes	No
Erosion.....	141	134
<i>Staphylococcus albus</i> .....	107	91
<i>Staphylococcus aureus</i> .....		1
<i>Staphylococcus citreus</i> .....		1
<i>Staphylococcus hemolyticus</i> .....	1	1
<i>Micrococcus flavus</i> .....	1	1
<i>Pneumococcus</i> .....	3	1
<i>Micrococcus pharyngis siccus</i> .....		1
<i>Micrococcus catarrhalis</i> .....	1	2
<i>Micrococcus tetragenus</i> .....	3	3
Large gram negative coccus unidentified.....	1	
Diphtheroid bacillus.....	15	11
Friedlaender's bacillus.....	1	1
<i>Bacillus lactis aerogenes</i> .....	1	
<i>Bacillus proteus</i> .....		2
<i>Bacillus subtilis</i> .....	14	17
<i>Bacillus xerosis</i> .....	1	
<i>Bacillus coli communis</i> .....	4	4
<i>Bacillus coli communior</i> .....	3	3
<i>Bacillus pseudodysentericus</i> .....	1	
<i>Bacillus fecalis alcaligenes</i> .....	2	
<i>Bacillus smegmatis</i> .....	5	
Gram positive bacillus unidentified.....	1	2
Gram negative bacillus unidentified.....		1
Gram positive spore bearing bacillus.....	1	1
<i>Bacillus mesentericus</i> .....		1
<i>Leptothrix</i> .....	16	18
<i>Streptothrix</i> .....	1	
<i>Nocardia</i> .....	1	1
Yeast cells and bacilli.....	10	12
<i>Streptococcus pyogenes hemolyticus</i> .....	2	2
<i>Streptococcus hemolyticus</i> unidentified.....	2	2
<i>Streptococcus hemolyticus anginosus</i> .....		1
<i>Streptococcus hemolyticus equinus</i> .....	1	
<i>Streptococcus mitis viridans</i> .....	10	12
<i>Streptococcus salivarius</i> .....		2
<i>Streptococcus fecalis</i> .....	1	2
<i>Streptococcus viridans</i> unidentified.....	5	2

The cultures were immediately taken to the laboratory where procedures were instituted to isolate and identify the organisms and their various strains. Following is a description of the laboratory technique used in isolating and identifying organisms from these cultures. The laboratory work was performed by two of us (J.W.McM. and G.S.L.). Two swabs were received from each patient. One was cultured aerobically, the other anaerobically. The aerobic cultures were streaked on blood agar and the swabs placed in the depth of sodium glycerophosphate veal broth tubes. This latter procedure was intended to facilitate anaerobic growth in the zones of reduced oxygen tension created around the swabs in the depths of the tubes. The tubes used were from 8 to 10 centimeters in depth. The anaerobic cultures were placed on blood agar and Loeffler's medium and the swab inserted into the depth of litmus milk tubes. Routine transfers to other media were re-

sorted to for specific identification. The anaerobic technique was that of a modified Wright's pyrogalllic acid method for approximately one-half the cultures. An anaerobic jar technique was used for the balance.

Aerobic cultures of the cervical secretion were made in each of the 275 patients. Attempts to cultivate organisms anaerobically were made only in the last 167 of the group.

The results obtained are tabulated on Table I. They demonstrate the usual multitude and variety of organisms which may be identified in any body cavity directly continuous with the environment and in which there is no well developed protective mechanism such as a highly bactericidal secretion. In only 37 of these patients were we unable to grow organisms by the usual cultural methods and of these aerobic and anaerobic efforts were made in 23. The 14 remaining were cultured only anaerobically.

Our laboratory uses the Holman classification of streptococci. The isolation of these organisms which is usually considered an index of potential pathogenesis was roughly proportional in the aerobic and anaerobic groups, i.e. 275:271:167:18.

Table II demonstrates an effort to determine whether erosion and mild chronic cervicitis constitute a predisposing factor to the occurrence of pathogenic organisms in the cervix or have any influence on their virulence.

From this analysis we must conclude: (1) that such changes in the cervix are not significant in so far as the occurrence of organisms is concerned (141 cases without erosion—215 organisms, 134 cases with erosion—199 organisms); (2) that they exert no influence on the presence of pathogenic organisms since streptococci were present about equally often with and without erosion (21:23, respectively); (3) that they surely do not predispose to postpartum infection since 12 morbid patients had cervical changes prepartum and 16 had normal cervixes. In other words, those patients whose cervixes were normal in appearance had a morbidity of 12 per cent, in contrast to a morbidity of 8 per cent in the group with erosion and mild chronic cervicitis.

In the light of our figures we believe that prophylactic measures to clear up such conditions of the cervix prepartum for the purpose of preventing intrapartum and postpartum infection are not indicated and may be even undesirable if they constitute a hazard, however slight, of inducing premature labor.

We made an effort to judge from our statistics whether multiparity had any relation to or influence on the occurrence of organisms in the cervix during pregnancy. Our results are tabulated in Table III.

They seem to indicate about an equal occurrence of organisms in pregnant women regardless of parity. There seems to be a somewhat higher incidence of streptococci in the cervixes of women during their earlier pregnancies. Results as far as morbidity is concerned are inconclusive because of the difficulty in determining the influence exerted by the greater number of operative procedures and manipulations incident to the delivery of first babies aside from the prepartum presence of cervical organisms. However, it seems fair to assume that the results of cervical trauma due to repeated childbirth do not promote a higher incidence of potentially pathogenic organisms in the pregnant cervix.

A study of the seasonal incidence of various organisms in the cervix is tabulated in Table IV.

An analysis reveals that there is about an equal total number of organisms present throughout the year. However, there is apparently an incidence of streptococci in the fall months (September, October, November) of about 1:6½, increasing in the winter (December, January, February, March) to about 1:5½, and decreasing in the spring and summer (April, May, June, July, August) to 1:10. It was interesting to find an expected increase in the isolation of organisms usually associated with respiratory infections during the months when they are most common.

We divided the patients in this series according to the stage of gestation in weeks as estimated from the approximate date of conception, using the last menstrual flow as our index. The results are tabulated in Table V.

It will be noted that the total number of organisms is proportional to the number of patients cultured at various stages of gestation. There seems to be a higher incidence of streptococci between the eighth and twentieth weeks with a rather definite and sharp drop thereafter. We note this without presuming to place any significance upon it. Errors in deduction are easily made if too many conclusions are drawn from a small series.

In evaluating our morbidity in conjunction with our prepartum cervical cultures, every effort was made to eliminate disturbing factors. All patients were delivered by or under the direct supervision of one of us (E. A. C. or D. L. O'L.). The delivery room routine was identical in each case in so far as vaginal and perineal preparation, etc. were concerned. No attempt has been made to correlate the occurrence of morbidity and the method of delivery, extent of interference, etc. as it is felt that in a series of 275 cases an average will be struck.

We consider our patients morbid if the temperature reaches 100.4 degrees F. on any 2 successive days of the puerperium excluding the first postpartum day. With this standard the morbidity of the entire series was 10.5 per cent—28 patients.

Six of these 28 were morbid from extragenital causes as: purpura hemorrhagica, paronychia, acute bronchitis, lobar pneumonia, artificial pneumothorax for old tuberculosis, postanesthetic pulmonary collapse after cesarean section.

In 11 of the remainder morbid according to the above standard, the pyrexia was of unknown origin, was unsustained, and all were discharged from the hospital by the twelfth postpartum day.

The remainder are summarized as follows:

(1) Five mild cases of septic endometritis of the

TABLE III.—EFFECT OF PARITY ON INCIDENCE OF ORGANISMS

Parity	I	II	III	IV	V	VI	VII	VIII	IX	X	XII	XIII	XV	XXI
No.	87	70	43	21	18	13	3	5	6	5	1	1	1	1
<i>Staphylococcus albus</i>	65	44	34	15	10	12	2	3	4	5				
<i>Staphylococcus aureus</i>	1													
<i>Staphylococcus citreus</i>			1											
<i>Staphylococcus hemolyticus</i>	2													
<i>Micrococcus flavus</i>	1	1												
<i>Pneumococcus</i>	1	1		1	1									
<i>Micrococcus pharyngis siccus</i>	1													
<i>Micrococcus catarrhalis</i>	1			1					1					
<i>Micrococcus tetragenus</i>	1	4		1										
Large gram negative coccus unidentified	1													
Diphtheroid bacillus	10	5	5	1		2			1	1	1			
Friedlaender's bacillus	1			1										
<i>Bacillus lactis aerogenes</i>		1												
<i>Bacillus proteus</i>	1			1										
<i>Bacillus subtilis</i>	9	11	3	2	1	2		1			1			
<i>Bacillus xerosis</i>	1													
<i>Bacillus coli communis</i>	1	2	2		1			1						
<i>Bacillus coli communior</i>	1	2	2	1		1								
<i>Bacillus pseudodysentericus</i>		1												
<i>Bacillus fecalis alcaligenes</i>	2													
<i>Bacillus smegmatis</i>	1	3		1										
Gram positive bacillus unidentified	1				2									
Gram negative bacillus unidentified	1													
Gram positive spore bearing bacillus	1	1												
<i>Bacillus mesentericus</i>					1									
<i>Leptothrix</i>	11	9	4	2	2	3		1	1		1			
<i>Streptothrix</i>		1												
<i>Nocardia</i>					1			1						
Yeast cells and bacilli	3	9	4	1	2							1	1	
<i>Streptococcus pyogenes hemolyticus</i>	3													
<i>Streptococcus hemolyticus</i> unidentified	2	1	1							1				
<i>Streptococcus hemolyticus anginosus</i>	1													
<i>Streptococcus hemolyticus equinus</i>			1											
<i>Streptococcus mitis viridans</i>	6	2	6	1	1	2	1	2						
<i>Streptococcus salivarius</i>	1		1											
<i>Streptococcus fecalis</i>		1	2											
<i>Streptococcus viridans</i> unidentified	3		2		1	1								

type that in the old literature would probably be called a sapremia. These patients recovered quickly and were all discharged from the hospital before the sixteenth postpartum day. (2) Three cases of infected perineal wounds, 2 of which re-

sulted from third degree extension of median episiotomies. These patients likewise were discharged by the end of the second week. (3) Two patients with acute pyelitis who had been in the hospital prepartum 2 days and 35 days and were

TABLE IV.—SEASONAL VARIATION IN THE INCIDENCE

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
	11	17	21	14	8	11	13	8	14	14	12	31
<i>Staphylococcus albus</i>												
<i>Staphylococcus aureus</i>			1									
<i>Staphylococcus citreus</i>						1						
Hemolytic <i>Staphylococcus</i>			2									
<i>Micrococcus flavus</i>							1			1		
<i>Pneumococcus</i>	1	2				1						
<i>Micrococcus pharyngis sacrus</i>			1									
<i>Micrococcus catarrhalis</i>		1		1								1
<i>Micrococcus tetragenus</i>		1					1	3				1
Large gram negative coccus unidentified		1										
Diphtheroid bacillus	3	5	1	1	1		1	1	1	1	1	1
Friedlander's bacillus									1	1		
<i>Bacillus lactis aerogenes</i>		1										
<i>Bacillus proteus</i>								1				1
<i>Bacillus subtilis</i>	6	4	6	3	1	1	1		1	1	1	
<i>Bacillus aerosis</i>	1											
<i>Bacillus coli communis</i>	1	2		1	1		1				1	
<i>Bacillus coli communior</i>				1	1	1	1	1				
<i>Bacillus pseudodysentericus</i>												1
<i>Bacillus fecalis alcaligenes</i>						1						
<i>Bacillus emegmatia</i>								1	1		1	
Gram positive bacillus unidentified		1			1							
Gram negative bacillus unidentified	1	1										1
Gram positive spore-bearing bacillus									1			
<i>Bacillus mesentericus</i>		1					1					
<i>Leptothrix</i>	3	4	3	1		1	1		1	4	1	4
<i>Streptothrix</i>	1					1						
NOBAC A										1	1	
Yeast cells and bacilli	6	3	4	1							1	1
<i>Streptococcus pyogenes hemolyticus</i>	1											
<i>Streptococcus hemolyticus unidentified</i>			3									1
<i>Streptococcus hemolyticus anginosus</i>											1	
<i>Streptococcus hemolyticus equisus</i>											1	
<i>Streptococcus mitis viridans</i>	1		3			1	3	1	1	3	1	3
<i>Streptococcus salivarius</i>		1										1
<i>Streptococcus fecalis</i>					1							
<i>Streptococcus viridans unidentified</i>	1	3	1							1		1
Number of patients per month	16	20	21	10	12	16	23	12	17	21	18	16

discharged 21 and 15 days postpartum, respectively. (4) One patient with femoral phlebitis with convalescence prolonged 12 days.

There was 1 maternal mortality in the group resulting from postpartum hemorrhage following

delivery for placenta previa. This patient had been packed and transfused but succumbed from shock 15 hours after delivery.

Of the 23 patients morbid because of genital tract infection, 7, or 31.5 per cent, had positive

TABLE V.—PERIOD OF GESTATION IN WEEKS

	4-7	8-11	12-15	16-19	20-23	24-27	28-31	32-35	36-39
<i>Staphylococcus albus</i>	5	21	20	23	32	31	31	19	5
<i>Staphylococcus aureus</i>			1						
<i>Staphylococcus citreus</i>									1
Hemolytic <i>staphylococcus</i>		1		1					
<i>Micrococcus flavus</i>					2				
<i>Pneumococcus</i>				1	2	1			
<i>Micrococcus pharyngis siccus</i>					1				
<i>Micrococcus catarrhalis</i>			1	1		1			
<i>Micrococcus tetragenus</i>			1	1	2	1			1
Large gram negative coccus unidentified					1				
Diphtheroid bacillus		5	3	4	6	3	3	2	
Friedlaender's bacillus							2		
<i>Bacillus lactis aerogenes</i>			1						
<i>Bacillus proteus</i>		1		1					
<i>Bacillus subtilis</i>		5	5	3	2	7	5	1	1
<i>Bacillus xerosis</i>		2							
<i>Bacillus coli communis</i>	1		1			3	2		1
<i>Bacillus coli communior</i>					2		2	1	
<i>Bacillus pseudodysentericus</i>				1					
<i>Bacillus fecalis alcaligenes</i>					1	1			
<i>Bacillus smegmatis</i>	1		1		3		1		
Gram positive bacillus unidentified					1		1		
Gram negative bacillus unidentified			1			1			
Gram positive spore-bearing bacillus			2						
<i>Bacillus mesentericus</i>						1			
<i>Leptothrix</i>		4	7	4	1	7	9	1	
<i>Streptothrix</i>								1	
<i>Nocardia</i>							2		
Yeast cells and bacilli		1		3	2	5	5	5	1
<i>Streptococcus pyogenes hemolyticus</i>			1	1	1				
<i>Streptococcus hemolyticus unidentified</i>		1	2	1					
<i>Streptococcus hemolyticus anginosus</i>				1				1	1
<i>Streptococcus hemolyticus equinus</i>		1							
<i>Streptococcus mitis viridans</i>		3	5	4	1	3	3	1	
<i>Streptococcus salivarius</i>				1			1		
<i>Streptococcus fecalis</i>							3		
<i>Streptococcus viridans unidentified</i>		2	1	1	2	1			
Number of patients	5	27	38	40	43	40	43	28	8

streptococci cultures from the cervix prepartum. Three were hemolytic, 2 definitely *Streptococcus pyogenes hemolyticus*. From an additional patient with a negative prepartum culture a pyogenic streptococcus was obtained from the lochia,

apparently proving definitely an exogenous infection.

Table VI presents the figures from the entire series with the object of discerning a relationship between the prepartum presence of nonhemolytic

and hemolytic streptococci and the occurrence of postpartum morbidity.

TABLE VI.—RELATIONSHIP BETWEEN PREPARTUM STREPTOCOCCI AND POSTPARTUM MORBIDITY IN 275 PATIENTS

	Morbidity	
	No	Per cent
Total number of cases—275	29	10.5
Excluding extragenital causes	22	8
Excluding extragenital causes and positive streptococcus cultures	15	5.4
40 cases with positive streptococcus cultures	7	17.5
37 cases with nonhemolytic streptococci	4	10.9
9 cases with hemolytic streptococci	3	33.3

It will be noted in the above that in 40 of the 275 patients, or 14.5 per cent, streptococci were isolated from the cervix. Nine of these were hemolytic streptococci, 3.3 per cent.

#### SUMMARY AND CONCLUSIONS

1. A multitude of various micro-organisms were cultured from the cervix during pregnancy.
2. Streptococci were obtained in cultures from 14.5 per cent, and in 3.3 per cent were hemolytic.
3. Erosion and mild chronic nonspecific cervicitis are not contributing factors to puerperal morbidity.
4. Cervical trauma incident to repeated child-bearing does not promote a higher incidence of potentially pathogenic organisms in the cervix.
5. The incidence of streptococci as well as the number of micro-organisms of the respiratory group increase during the months when respiratory infections are more common.

6. There seemed to be a definite but perhaps not significant decrease in the incidence of positive streptococcal cervical cultures after the twentieth week of gestation.

7. Morbidity is somewhat higher in cases in which the cervix harbor streptococci, especially if these organisms promote hemolysis.

8. Endogenous infection from the cervix does occur but in the present series has been exceedingly mild and of short duration.

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# DACRYOCYSTORRHINOSTOMY

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**D**ACRYOCYSTORRHINOSTOMY is not a new procedure; its use has been reported periodically since the time of Platner (10, 1724). The operation is not easy but, once mastered, it gives such a satisfactory re-establishment of the normal physiology that, in the great majority of cases of obstruction of the nasolacrimal duct, there can be little excuse for removal of the lacrimal sac. The patient and surgeon should be content with nothing less than this desirable result. A definite classification of the results based on certain tests is proposed.

Many different methods have been used approaching through a skin incision or intranasally, or even through the antrum.

Ohm in 1920 made an important contribution, operating through an external incision. Instead of removing the sac wall or nasal mucous membrane, he fashioned anterior and posterior flaps from them and attached them to each other by means of sutures. In 1921 Dupuy Dutemps described a similar procedure. This operation we will describe later in greater detail; it has proved itself a worthy procedure. Direct continuity was thus established by surgically joining the nasal mucous membrane to wall of the lacrimal sac.

In 1938 one of us (L. G.) described what he termed "simple dacryocystorhinostomy" which very closely resembled the technique originally described by Montaigne in 1836. The results were not permanently satisfactory in sufficient cases to warrant continuation of this method.

We felt that the method of making the flaps was relatively unimportant. In our series, and in the cases reported in the literature, the results were uniformly superior when the flaps were definitely sewn in position to form a continuous mucous membrane bridge for new bony canal.

## INDICATIONS

1. The operation is indicated when there is obstruction of the lacrimal drainage apparatus at the lower portion of the lacrimal sac or nasolacrimal duct in the absence of acute inflammatory reaction. The presence of a chronic infection in the sac does not contraindicate the operation unless the infection is tuberculous. Even the

presence of a tense mucocele is not an absolute contraindication. If the sac can be entered easily with a blunt cannula or probe there is probably not a cicatricial obstruction of the canaliculi.

2. In the presence of trauma when part of the lacrimal sac remains and the canaliculi are intact.

3. When after a partial removal of the lacrimal sac a moderate amount of discharge persists.

4. After a dacryocystectomy, a repair may be done according to the technique of Arruga by implantation of the end of the canaliculus, which has been dissected free, into the nasal mucous membrane.

As a preliminary to intra-ocular operations, the reestablishment of the flow of the lacrimal secretion through the conjunctival sac into the nose is preferable to dacryocystectomy because it results in a cleaner eye with fewer organisms than are found with the stagnation that must follow extirpation. This was proved by the work of Mattice reported in 1931. He found pneumococci in 43 per cent of conjunctival sacs after extirpation, while Bumke and West (9) found that pathological organisms disappeared from the conjunctiva soon after re-establishment of drainage through the sac.

## CONTRAINDICATIONS

1. The operation is contraindicated when there is irremediable obstruction to the puncta or canaliculi in any part, especially at the entrance to the sac.

2. When malignant disease involves the sac.

3. When the mucous membrane lining the sac has been destroyed by an incurable condition, such as tuberculosis, actinomycosis, or malignancy.

4. When there is present extensive nasal disease with obstruction in the region of the anterior end of the middle turbinate where the new opening is to be made, or sinusitis is present with emphasis on the ethmoids. When polypi, obstructions in this region, or sinusitis are eliminated, the procedure may be carried out.

5. When acute inflammation is present. When this subsides the operation may be done. Chronic infection of the sac is not a contraindication.

## TECHNIQUE

1. *Preparation.* Infection in the lacrimal sac is treated. If any acute inflammation is present, the

From the Research Department of the New York Eye and Ear Infirmary.



TABLE I.—COMPARATIVE RESULTS WITH AND WITHOUT SUTURES, BY ALL METHODS AND ALL OPERATORS

Dacryocystorhinostomy					
Test		Successes		Failures	
		Cases	Per cent	Cases	Per cent
Mercurochrome (gravitating into nose without force in 2 to 30 minutes)	Sutures	12	81.4	3	5.4
	No sutures	6	10.7	34	60.7
(Cross or seen intranasally)	Dams	1	1.8	0	
Total		19	33.9	37	66.1
Total successes and failures				56	
Mercurochrome plus irrigation	Sutures	17	21.3	4	5.3
	No sutures	13	17.1	38	50.0
	Dams	3	4.0	1	1.3
Total		33	43.4	43	56.6
Total successes and failures				76	
Totals based on patients' statement that there is no pus but slight or some epiphora		50	53.7	43 known	46.3
Total successes and failures				93	

contents of the sac may usually be gently aspirated through either upper or lower canaliculus and the sac carefully washed out. Subsequently mercurochrome and hot compresses are used. When the inflammation has subsided the first form of dacryocystorhinostomy, i.e. probing, may be attempted. This can usually be done almost painlessly if the anesthetic (2 per cent pontocaine or 4 per cent cocaine) with ephedrine, with which the sac is filled at 10 minute intervals, is allowed to remain in the sac a sufficient length of time—at least 20 minutes. Hypodermic injection of 2 or 3 drops of 4 per cent novocain into the nasal duct is occasionally necessary for complete anesthesia. If drainage is not reestablished by two or three probings, further attempts are usually futile. We have had little experience with retained probes or cannulas.

When the reestablishment of drainage through the normal duct becomes impossible, a new opening, properly constructed, serves the purpose very well. The preliminary probing and treatment serve to reduce the severity of the pyogenic infection in the sac in preparation for the operation. It may be carried out, however, in the presence of a chronic pustular condition without danger of complicating infection, if the sac is aspirated and washed out at the time of operation.

TABLE II.—GENERAL SURVEY OF DATA IN CASES OF LACRIMAL SAC DISEASE REGARDING AGE AND SEX

General			
Sex	Average ages*	Number of cases	Per cent of cases
Males	47.03	83	24
Females	44.50	264	76
Total cases	45.70	347	100

\*Youngest, 4 weeks, oldest, 80 years

Dacryocystorhinostomies			
Sex	Average ages*	Number of cases	Per cent of cases
Males	55.40	27	25
Females	41.60	82	75
Total cases	48.50	109	100.4

\*Youngest, 4 years, oldest, 75 years

Extirpations			
Sex	Average ages*	Number of cases	Per cent of cases
Males	47.50	33	24
Females	48.02	105	76
Total cases	47.76	138	100.0

\*Youngest, 4 years, oldest, 75 years

Nonsurgical			
Sex	Average ages*	Number of cases	Per cent of cases
Males	38.20	19	51
Females	43.90	93	83
Total cases	41.05	112	100.6

\*Youngest, 4 weeks, oldest, 80 years

The nose should be checked over first to see that there is no gross obstruction or infection present.

2. *Lighting.* Besides general illumination of the operative field, a good headlight, arranged so the vision is along the axis of the illuminating beam, is essential.

3. *Anesthesia.* a. *Local.* The corresponding naris is sprayed with 4 per cent cocaine solution and the upper part packed with a cocaine soaked pledget in the region superior and anterior to the middle turbinate. The skin is injected with 4 per cent novocain to which is added 2 drops of 1:1000 solution of epinephrine hydrochloride for each 5 cubic centimeters. A No. 27, half inch needle is employed. Next, with a longer needle, 1 1/2 cubic centimeters of the same solution is injected well behind the dome along the nasal wall of the orbit directly against the periosteum. In a similar manner an injection is made behind the lower portion of the sac, and finally the needle is directed into the entrance to the nasolacrimal duct.

and 0.5 of a cubic centimeter is injected. One can easily enter the bony canal by palpating the anterior lacrimal crest on the opposite side and by directing the needle from above to a symmetrical location on the involved side.

b. General. Preliminary sedation with 4.5 to 6 grains of nembutal for the average adult is given by mouth 15 minutes before operation. If a general anesthetic is employed, a postnasal plug is used.

4. *Operative procedure.* A 15 millimeter arcuate skin incision is made, starting 3 millimeters nasal to and 4 millimeters above the medial canthus. This is carried down to the periosteum. A speculum is then placed to keep the wound open. The medial canthus is straddled with a Lester forceps, and its medial attachment is severed completely at the point where it spreads out after passing over the upper portion of the sac to be attached to the periosteum nasally. The dome usually extends above the upper portion of the ligament although occasionally it does not. The superficial layer of the deep or tarso-orbital fascia is incised along its attachment to the anterior lacrimal crest, hugging the bone tightly to avoid injury to the sac. This anterior lacrimal crest which can be readily felt by palpation is the outstanding landmark; the sac is always to be located directly behind this bony ridge. If there is any doubt as to the presence or integrity of the walls or the location of the sac, as in traumatism with fracture cases, or if previous surgery has been attempted, it is well to aspirate the contents of the sac and inject *very gently* 2 or 3 drops of methylene blue in order to identify its wall later. This latter procedure should not be done directly after probing.

The sac, which is easily identified by its bluish color, is pushed temporally and an opening is made in the bone starting along the anterior crest. The opening can be made with chisel and hammer which can be supplemented, if desired, by a 4 millimeter hand bone trephine. The rapidly revolving automatic electric trephines are not as safe or satisfactory. Soft tissues may become wrapped around the revolving end and serious damage result before the machine can be stopped. Another danger from the electric trephine is damage to the nasal mucous membrane, which is rarely injured when the hand chisel and mallet are used. When the opening is sufficiently large to admit a small size bone-cutting forceps of the Citelli or Kerison type, this instrument is used to clip off the margins to enlarge the opening to about 1.5 centimeters in diameter. A sharp mastoid curette is sometimes useful for this purpose. In making the bony opening, an ethmoid

cell may be encountered. This can be determined by inability to see into the nasal cavity and terness of the mucous membrane lining it. When thick nasal mucous membrane is identified and bony opening is sufficiently wide, all the bony chips are removed and the edges of the opening smoothed off. In making the osseous window, usually encounters the anterior end of the middle turbinate, and the opening in the mucous membrane is planned either superior and anterior to this structure or inferior to it.

The incision in the nasal mucous membrane is then made in the shape of an H with a long horizontal bar so planned that the two flaps outline by the upper and lower halves of the H will correspond flaps from the sac. The postnasal flaps are united by two plain catgut No. 5 sutures. These are not easily applied in some cases, but small Yankauer needles, if well sharpened, are of help. Occasionally the posterior flap cannot be united. This is not of much importance if the anterior flaps are brought together. The wound is closed with interrupted black sutures, one suture passing through the medial canthal ligament as well as the skin. At the end of the operation, the cornea should be inspected for traumatism by instillation of a drop of rescin and the conjunctival sac should be flushed to remove any infectious material. A preservative dressing is applied, particular attention being paid to the proper alinement of the lashes. It is changed in 24 hours in order to allow inspection of the cornea but is reapplied and left in position for a week, after which time a light dressing may be used for another week or so. There is practically no postoperative reaction.

#### COMPLICATIONS IN THE OPERATIVE TECHNIQUE

1. *Hemorrhage.* This usually complicates the operation in four stages and may be checked in the following ways: (a) Just after making the incision, hemorrhage is often controllable by changing the position of the prongs of the speculum or by small hemostatic forceps, compressing the vessels or bleeding points. (b) While making the window in the bone, it is sometimes controllable by pressure or packing with adrenalin soaked gauze. Actual cautery or diathermy with coagulation current may be necessary. The hemorrhage at this stage is most annoying and interferes with the dissection. A small suction tip can be used to great advantage in keeping the field clean. A slightly bent plain-tipped dropper makes a good tip for this purpose. Occasionally when the nasal mucous membrane is incised, hemorrhage occurs. It is usually f

COMPARISON OF DACRYOCYSTECTOMY  
WITH DACRYOCYSTORHINOSTOMY

Dacryocystectomy	Dacryocystorhinostomy
1 Eliminates pustular discharge and infection	Same
2 Does not eliminate overflow of tears	Eliminates overflow of tears
3 Does not reestablish the normal drainage of the impurities and secretions of the conjunctival sac	Reestablishes the normal drainage
4 Very difficult to reestablish drainage if the sac is completely removed	May be repeated with hope of success in the occasional case where the drainage opening closes
5 Operation is final	Dacryocystectomy may still be done if necessary
6 Patient usually complains about the remaining tearing and is not completely satisfied	Patient is usually completely satisfied
7 Dacryo-adenectomy or other procedure is often required to reduce the tearing	Other operations are rarely necessary
8 Simpler operation	Considerably more difficult operation
9 No air regurgitation possible	Cases have been reported in which air is forced back through the canaliculus on blowing the nose. This was not seen in any case of our series but undoubtedly it may occur

easily controlled by packing the wound although rarely the packing may need to be done from the nose as well. (d) Late hemorrhage occurring a few hours after the operation is rare and has not been seen by any of us. Packing of the nose is indicated with, possibly, cauterization of the bleeding point.

2. *Dissection.* One should hardly need to mention failure to locate the sac. This failure is most easily avoided by first locating and completely severing the attachment of the medial canthal ligament nasally and by palpation of the anterior lacrimal crest with the finger. This is always palpable and the sac is always located just posterior to this bony crest.

3. *Injury to the sac during dissection.* This is most easily avoided by cutting through the tarso-orbital fascia directly at its attachment to the periosteum along the anterior lacrimal crest. If the sac is incised, it is usually not serious as the incision can generally be extended to form the flap. If more extensive damage is done, enough sac wall can be salvaged to unite at least one lip of the nasal mucous membrane. In fact, the incision in the nasal mucous membrane may be changed to provide one longer flap if necessary.

COMPARISON OF INTRANASAL PROCEDURE  
WITH EXTERNAL OPERATION

Intranasal operation	External operation
1 Limited operating field	Better exposure of operating field
2 Frequently requires preliminary removal of a deviated septum and almost always removal of the anterior tip of the middle concha	Rarely requires any intranasal surgery except in cases of gross pathology or complete obstruction
3 Intranasal granulations must frequently be treated after operation	No traumatism to the intranasal structures
4 Postoperative scarring of the nasal mucous membrane with its resultant formation of dried secretion and scabs at the site of the scar	No damage or alteration of nasal mucous membrane
5 Operation in the field of the rhinologist	Operation in the field of the ophthalmologist who almost always sees these patients first and who can also relieve other pathological condition of the lacrimal apparatus when necessary

One well formed flap united to one sac edge will provide a permanent drainage tract into the nose.

4. *Disease of the nasal mucous membrane.* This is occasionally present, making handling difficult. This complication can be avoided often by preoperative treatment of the nose and sinuses. The nasal mucous membrane may be quite fragile making it impossible to form proper flaps to unite to the sac. In this case the sac should be dissected free and cut off at the lower part. A suture should be passed through the margin of the lower cut edge of the sac, through the bony opening, and brought out through the nostril, the lower end of the sac should be pulled into the nose and the suture anchored to the cheek, as originally done by Forsmark in 1911.

5. *Failure of the newly created duct to function.* This may be due to (a) injury to the canaliculus at the time of the operation, or (b) closure of the osseous opening on account of (1) insufficient size or improper placement of the fenestra in the first place, or (2) lack of proper apposition of the nasal mucous membrane and the lacrimal sac flaps. In this case a probing through the new opening may be attempted and, if this is unsuccessful, the entire operation may be repeated with good prospect of success.

6. *Postoperative complication.* A case in which a corneal ulcer developed before the first dressing on the third day, resulting in some corneal opacity, has been observed. This was probably due to in-

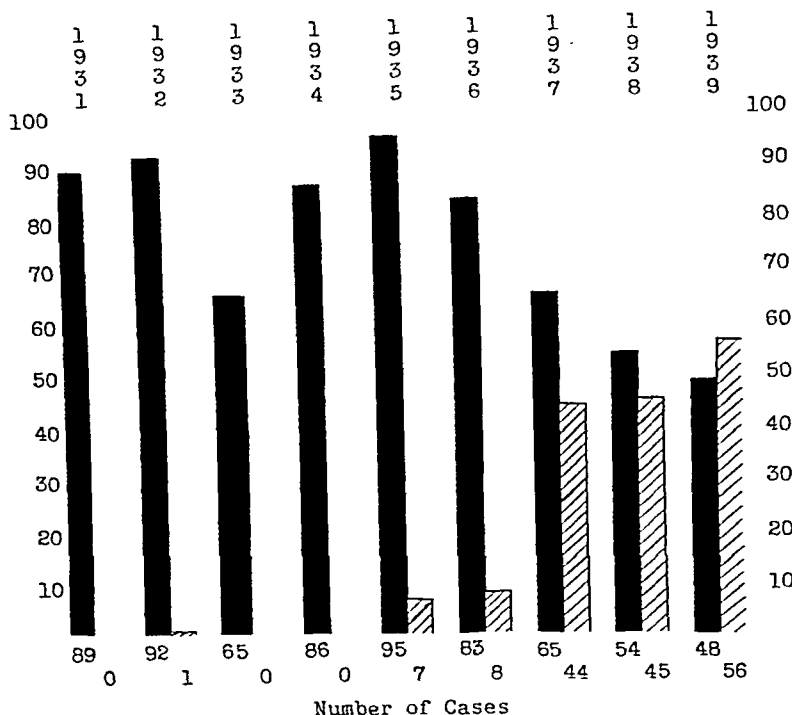


TABLE III.—Tear sac operations at New York Eye and Ear Infirmary. Black areas, dacryocystectomies; cross hatched areas, dacryocystorhinostomies.

complete cleansing of purulent discharge from the conjunctival sac before the dressing was applied. The pressure dressing may have been applied too tightly or the lashes may have been inverted against the cornea by the dressing.

#### CRITERIA USED TO JUDGE SUCCESS OF THE OPERATION

Most surgeons in reporting their cases, especially those reporting nearly one hundred per cent successful operations, fail to mention what criteria were used. It is felt that some standard should be set up for this purpose.

1. *Clinical relief of symptoms:* (a) the absence of tearing should be specifically stated whether or not it is absent at all times and especially in the cold and the wind. The result can not be judged as "completely successful" unless there be no more tearing of the affected eye than there is in the other eye, if the other lacrimal drainage apparatus is normal. (b) The absence of discharge is a distinct advantage to be gained but is also obtained by a well performed dacryocystectomy.

2. *Physiological instillation test.* (a) The most severe test is the instillation at a 3 minute interval

of two drops of mercurochrome or other dye into the conjunctival sac and ascertaining its presence in the nasal cavity by blowing the nose 10 to 20 minutes later. The stain will normally appear on the handkerchief. (b) It may be necessary for a time to instill 2 drops of vasoconstrictor to reduce the congestion of the mucous membrane lining the lacrimal passage before the dye will pass into the nose spontaneously. This method of treatment will frequently result in a healthier mucous membrane and establishment of spontaneous drainage. Unless spontaneous drainage without the use of vasoconstrictor be established, the case can not be classified as "completely successful."

3. *Irrigation test.* Saline will pass into the nose by irrigation, administered by means of a curved lacrimal cannula or a glass syringe inserted into the punctum, provided there is no dense stricture. This does not mean that spontaneous drainage of the tears has been established.

4. *Irrigation after probing.* Probing of the new passage is relatively easy and will be necessary if the new opening closes. The probe is passed through the new bony ostium. Permanent drainage may sometimes be established in this manner

if the opening has been closed only by means of mucous membrane. However, if the bony opening closes by means of dense scar tissue or a new growth of bone, the entire procedure must be repeated. In rare instances dacryocystectomy must eventually be performed, although in our series this was not done in any case.

#### CLASSIFICATION OF RESULTS BASED ON THE ABOVE CRITERIA

1. (a) *Complete success* Both clinical relief and proof of the reestablishment of normal physiology (by instillation test).

(b) *Partial success.* Relief from the excessive discharge with continuation of any tearing. These cases may become "completely successful" after treatment.

2. (a) *Complete success.*

(b) *Partial success.* Slight tearing in wind or some tearing with absence of discharge.

3. *Partial success.* Same as 1 (b).

4. *Complete failure.* No relief of tearing or discharge.

At the New York Eye and Ear Infirmary, dacryocystorhinostomy was practically unknown before 1931. Since 1934 the number of dacryocystorhinostomies has rapidly increased and dacryocystectomies decreased until today the number of the former being performed surpasses the latter (see Table III). This is a healthy trend

and more and more patients with an atresia of the lacrimal duct are demanding the advantages of this former operation with its relief of all signs and symptoms rather than simply relief from the infectious process present in the lacrimal sac. It has often been asserted that the surgeon is content with the results of dacryocystectomy. To this may be added that the patient is rarely completely satisfied.

In a study of all the cases of dacryocystorhinostomy done at the New York Eye and Ear Infirmary by various operators, the highest percentage of successful cases was obtained when the nasal mucous membrane and lacrimal sac flaps were united by suture. These statistics are also borne out by a review of the cases reported in the literature.

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# ATRAUMATIC AMPUTATION THROUGH THE LOWER THIGH (CALLANDER)

## Modified Technique

FELIX L. PEARL, A.B., M.D., San Francisco, California

IN 1935, Dr. C. L. Callander became strongly impressed with the severe shock and high mortality of lower thigh amputation performed according to the usual technique which transects the large thigh muscles through their fleshy portions. His results were especially unsatisfactory in those cases in which there was infection with anaerobic gas-producing bacteria, and he believed that the opening of large muscle spaces was an important factor contributing to the spread of infection up the stump. In an effort to avoid the high mortality of the usual muscle-cutting thigh amputation, Callander devised a technique which represented a great advance in the surgery of amputations. In this new technique no muscle bellies were cut; all sections of muscles were made through their tendinous insertions. The skin flaps were made very loose. The patella was excised and its bed made available as a cover for the bone end. As the skin flaps retracted snugly about the bone, the hamstrings pulled the suture line posteriorly and proximally and drew the patellar bed over the end of the stump. For further details the reader is asked to consult the original articles (1, 2).

In commenting on the anatomical basis for his operation, Callander presents certain pertinent facts: (1) The popliteal fossa is in reality a closed cavity, the intact upper limit of which acts as an effective barrier to the spread of infection up the thigh. This bulwark is preserved if muscles are cut only through their tendinous portions but is destroyed in the operation which cuts the fleshy portions. (2) The deep femoral artery nourishes the tissues of the thigh, and the skin and subcutaneous tissues of the knee and upper leg. It is rarely affected by occlusive arterial disease even when the femoral artery and its continuation, the popliteal, are completely blocked by the process. This allows the fashioning of long viable flaps from the skin and subcutaneous tissues of the upper leg in the majority of cases of advanced occlusive arterial disease. These considerations are

especially important in amputation for vascular disease, when the control of the spread of infection and the complete absence of tension are cardinal requisites for a successful outcome.

The following additional considerations recommend the operation for peripheral vascular disease: (1) The omission of the tourniquet eliminates possible further injury to an embarrassed peripheral circulation. (2) The absence of shock is noteworthy. (3) The ability to sit up in a chair within 1 to 3 days is a great preventative against stasis in the general and pulmonary circuits in old and debilitated patients. (4) The control of the circulation of the extremity is effected early, thus curtailing the return of contaminated blood and reducing the amount of arterial bleeding. (5) The stump is long, mobile from the first, practically painless, bears the body weight well on its end, and is easily fitted with a satisfactory prosthesis.

Because of these favorable points, the new type of amputation was employed by the Mt. Zion clinic of sympathetic and vascular surgery for the first time in 1936. The results were so gratifying that it was soon adopted as the routine lower thigh amputation in the clinic. Our experiences with the Callander type of amputation are being reported in detail in another article. It is sufficient here to remark that the results were far more satisfactory than those in which the orthodox technique was employed.

Despite the low mortality, certain points in the course of the new amputation required further study. The percentage of delayed healing was considerable; edema of the stump, even in cases which healed per primam was frequent and persistent; and the patellar bed sometimes formed a mobile mass which did not fit snugly over the bone and interfered with the satisfactory use of the prosthesis.

In those cases in which necrosis of the deeper tissues occurred the patellar recess appeared to be the area most often and most profoundly affected by the process. This may have been due to the fact that the peripatellar tissues are, as a rule, poorly vascularized, especially in patients suffering from arterial insufficiency. This area, too, is

From the Clinic of Sympathetic and Vascular Surgery, service of Dr. Harold Brunn, Mt. Zion Hospital, San Francisco, California.

if the opening has been closed only by means of mucous membrane. However, if the bony opening closes by means of dense scar tissue or a new growth of bone, the entire procedure must be repeated. In rare instances dacryocystectomy must eventually be performed, although in our series this was not done in any case.

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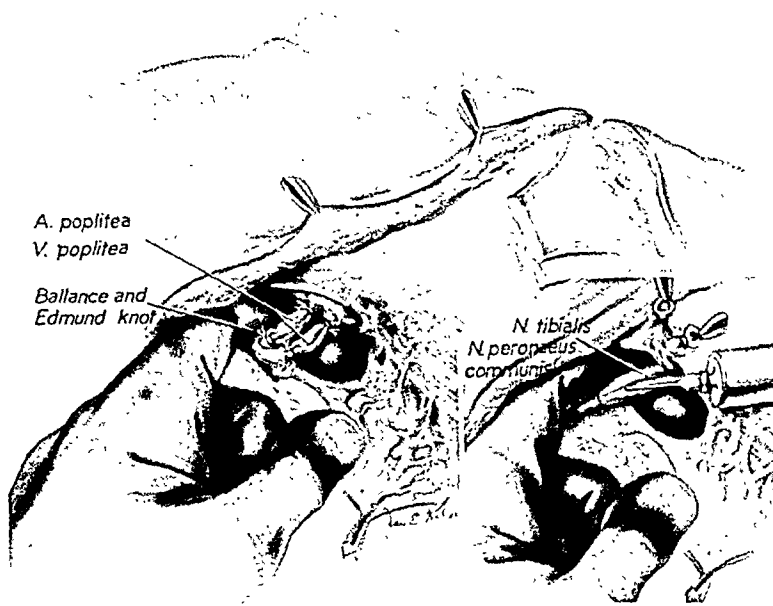


Fig. 3. Treatment of vessels and nerve. The popliteal vessels are withdrawn from the wound and cleansed of extraneous tissue. The adventitia is stripped of both artery and vein for a distance of about 1 inch. The distal portion of the vein is ligated first with No. 1 silk. The proximal portion of the vein is then ligated. The artery is treated by placing a Ballance and Edmund knot on the proximal end and an ordinary ligature on the distal end. Section is made between ligatures. The inset shows the tibial and common peroneal nerves cleansed of surrounding tissue and ligated high with a ligature of No. 0 plain catgut. A fine needle is shown inserted for the injection of absolute alcohol. The divided blood vessels are visible. Section of the nerve is performed through the alcoholized area. It may be necessary to ligate the distal portion of the nerve to control bleeding from the arteria comitans nervi ischiadici.

with scratches used as landmarks. Note that from the proximal limits the anterior and posterior incisions diverge promptly and form flaps of equal size and shape. This allows for more accurate approximation without the sacrifice of the cardinal principle of absolutely loose flaps. It seems that retraction of the posterior flaps is greater in thin extremities than in those with more subcutaneous tissue. It is wise, therefore, to make the posterior flap about 1 centimeter longer in thin individuals. Should amputation be desired through the bone, from 2 to 4 inches above the epicondyles, the flaps are merely fashioned at a correspondingly higher level. The incisions are developed through the skin, subcutaneous tissues, and deep fascia both on the anterior and posterior flaps.

*Tenotomy of medial hamstrings.* The tendinous insertions of the hamstring muscles on the tibia are exposed and sectioned as shown in Figure 2. These tendons should not be mobilized above the site of section. If the amputation is to be done

well above the epicondyles, the site of section should be high in the purely tendinous portion of the muscles. Thus the attachments of musculus sartorius, gracilis, semimembranosus and semitendinosus are divided.

*Entry into the popliteal fossa and treatment of vessels and nerve.* The cleft between the vastus medialis and the sartorius is deepened, the deep fascia is split, and the popliteal fossa entered. The forefinger is inserted with its dorsum uppermost, hooks around the popliteal artery and vein, and draws them out into the superficial tissues. The delivery of the vessels and nerve is facilitated by maintaining the knee in slight flexion. The vessels lie close to the posterior surface of the femur (Figs. 3 and 9). The vein is treated first so as to prevent contaminated blood from feeding the general circulation. It is freed from the artery by sharp and blunt dissection, its adventitia removed for a distance of about 1 inch and the vein sectioned between two ligatures of No. 1—Deknatel—silk applied with carrier. The artery is similarly



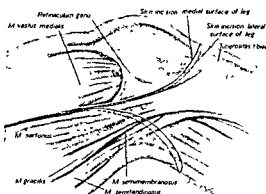


Fig. 1. Flaps of skin and subcutaneous tissue are marked out as shown. Note that flaps are of approximately equal length and that only about 1 centimeter of the proximal end is common to both flaps.

of necessity subjected to considerable trauma in separating the patella from the intimately attached peripatellar tissues. The retention of the peripatellar tissues to form a cushion for the bone end was stressed in the operation as described by Callander. In the older muscle transecting type of technique, even though fascia and muscle were used to cover the bone, these structures soon atrophied, thus leaving the bone end covered only by skin and a small amount of subcutaneous tissue. Despite this, satisfactory end-bearing was achieved. The necessity, and even the advisability, therefore, of retaining the patellar bed is open to question. These apparent disadvantages in no way detract from the soundness of the basic principles underlying the Callander technique. They act rather as a challenge to modify and, if possible, improve the desirable operation of low thigh amputation which transects tendons only.

The author offers herein a modified technique which has been developed in an effort to eliminate some of the disadvantages noted above. In short, the modification consists in (1) a change in the outline of the skin flaps, (2) removal of the patella and the peripatellar tissues, and (3) higher bone section through the medullary portion of the femur. It has been used on 14 cases with 1 death resulting from cardiac failure in a man of 73 years. These modified amputations, as well as other earlier amputations by use of the original Callander technique, have been performed by the author on patients suffering from affections of the peripheral arteries. The results of the modified amputation appear to offer advantages over the original technique in (1) the tendency to heal *per primam*, in (2) the contour of the stump, and in (3) the abil-

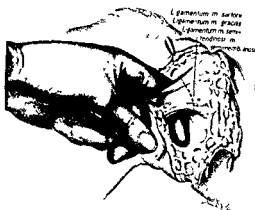


Fig. 2. Section of medial hamstring tendons. The flaps have been marked out and dissected so as to expose the tendons of the hamstring muscles at their insertions. The finger is slipped under the hamstring tendons preparatory to section.

ity to use prosthesis. The steps in the operation follow.

#### OPERATIVE PROCEDURE

**Preparation of the field.** A sterile dressing is applied to the foot and the lower half of the leg and bandaged firmly. This is subsequently not disturbed. The entire extremity is shaved from the groin to the midleg, cleansed with ether and alcohol, painted with tincture of merthiolate, and wrapped in a sterile towel. In the operating room the chemical preparation is repeated with care not to draw sponges from the lower portion of the field toward the site of operation. The area previously bandaged is redraped, bandaged, and covered with a sterile stockinet. The draping is carried out so as to allow free movement of the extremity.

**Fashioning of the flaps.** The operator stands facing the medial aspect of the knee joint. The joint is flexed about 15 degrees, held laterally by the first assistant, and supported in slight flexion by the second assistant. The flaps are marked out as follows: A scratch is made 3 fingers' breadth above the upper limit, respectively, of the medial and lateral epicondyles to mark the proximal limits of the incision, another about 1 centimeter above the tibial tuberosity to mark the distal limit of the anterior flap, a fourth in the center of the posterior aspect of the upper third of the leg at the same level as the distal limit of the anterior flap, to mark the distal limit of the posterior flap. The flaps are fashioned as shown in Figure 1.

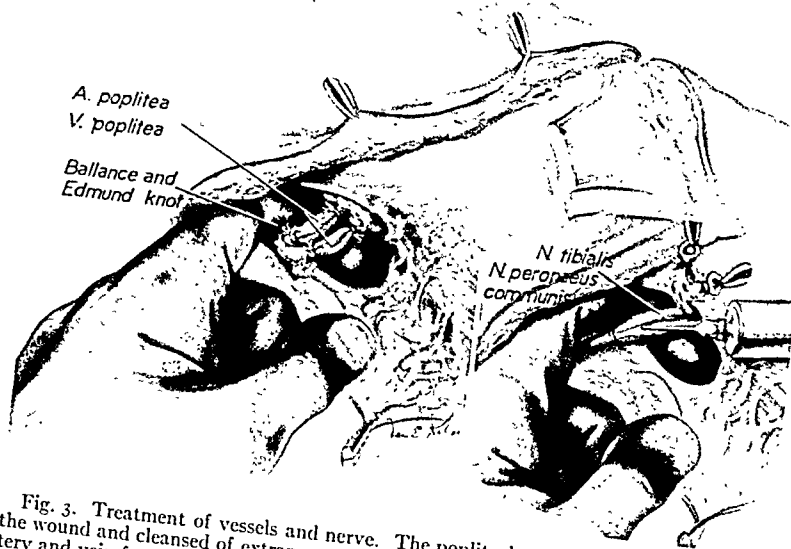


Fig. 3. Treatment of vessels and nerve. The popliteal vessels are withdrawn from the wound and cleansed of extraneous tissue. The adventitia is stripped of both artery and vein for a distance of about 1 inch. The distal portion of the vein is ligated first with No. 1 silk. The proximal portion of the vein is then ligated. The artery is treated by placing a Ballance and Edmund knot on the proximal end and an ordinary ligature on the distal end. Section is made between ligatures. The inset shows the tibial and common peroneal nerves cleansed of surrounding tissue and ligated high with a ligature of No. 0 plain catgut. A fine needle is shown inserted for the injection of absolute alcohol. The divided blood vessels are visible. Section of the nerve is performed through the alcoholized area. It may be necessary to ligate the distal portion of the nerve to control bleeding from the arteria comitans nervi ischiadici.

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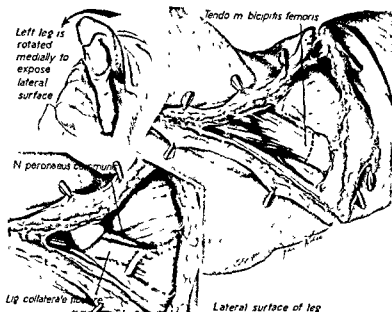


Fig. 4. Section of tendon of the musculus biceps femoris. The knee is rotated toward the operator to expose the lateral surface of the joint. The tendon of the biceps femoris is shown and its site of section indicated. Some of the tendinous fibers of the iliotibial tract must be divided. The upper inset shows how the leg is rotated toward the surgeon. The lower inset shows the biceps tendon sectioned and the common peroneal nerve exposed. This nerve has already been treated higher in the popliteal fossa.

denuded and sectioned between ligatures of the same material, except that the proximal portion is best ligated with a Ballance and Edmund knot, two contiguous strands of the same material being used (Fig. 3). This knot does not slip easily and tends to prevent fracture or cutting of the arterial wall. A carefully placed ordinary triple throw square surgical knot may be used if desired. If the artery pulsates it is wise to anchor the proximal ligature with a through-and-through embracing mattress suture of B—Deknatel—silk through all the arterial coats. If the vessel is soft and transmits considerable blood, it is best to compress it temporarily above while the ligature is being slowly drawn home, care being taken not to fracture the arterial coats with too much force. The tibial and common peroneal nerves are then with drawn as one trunk from the popliteal fossa and cleansed of all extraneous tissue. The nerve trunk is ligated as high as possible with No. 0 plain cat gut, injected distal to the ligature with absolute alcohol (Fig. 3, inset), and sectioned with a razor blade. The ligature serves the triple purpose of (1) preventing bleeding from the arteria comitans nervi ischiadici, which is a greatly augmented collateral in chronic occlusions of the femoral artery,

(2) preventing alcohol from traveling up the nerve, and (3) keeping the effect of the alcohol localized. When higher amputation is contemplated, section of vessels and nerve is made correspondingly higher.

*Tenotomy of musculus biceps femoris.* Without changing his position the operator rotates the extremity toward him to expose the lateral side of the knee joint (Fig. 4). The cleft between the biceps femoris and the iliotibial tract is deepened and the biceps traced to its insertion, the skin flaps being dissected so as to give the necessary exposure. The biceps is sectioned through its tendon (Fig. 4), but at times the muscle fibers come very low and a few must be cut as the tendon is sectioned.

*Scalping back of the anterior flap and mobilization of the posterior flap.* The dissection of the anterior flap is then carried through the deep fascia to the tissue compartment between the deep fascia and the ligamentum patellae. The scalping procedure can now be executed with dispatch. The surgeon grasps the free end of the anterior flap gently but firmly in both hands and scalps the anterior flap in a single sweep back to the level of the superior border of the patella (Fig. 5). There

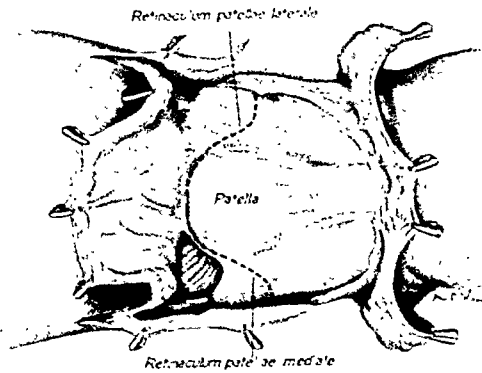


Fig. 5. Scalping back the anterior flap. The anterior flap has been scalped backward and the superior border of the patella exposed. The site of section of the tendon of the quadriceps and the retinaculum genu are indicated.

is usually no bleeding. The incision marking the posterior flap is deepened to the fascia covering the gastrocnemius and dissected free of the muscle up to a point above the attachments of the gastrocnemius heads.

*Entering of the knee joint through the suprapatellar bursa and section of the retinaculum genu.<sup>1</sup>*

<sup>1</sup>Otherwise known as retinaculum patellae, mediale or laterale. Author prefers "genu" as structure in mind is associated more with knee joint proper than with patella alone and extends far laterally and distally from patella.

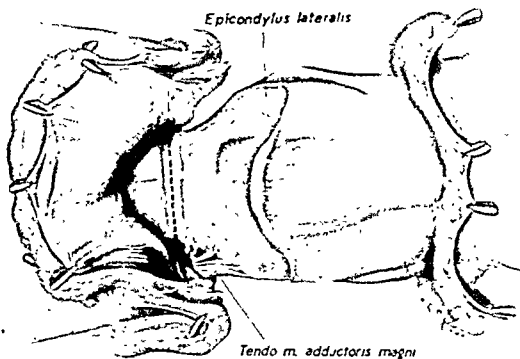


Fig. 7. Exposure of site of proposed amputation. Preparation of bone for section. The posterior flap has been dissected free of the gastrocnemius muscle to above the gastrocnemius heads. The retinaculum genu has been cut. The tendon of the adductor magnus has been sectioned. The areolar tissue and periosteum covering the bone have been divided and dissected for a distance of about 1 centimeter at the site of proposed amputation. Gauze tapes covering the soft tissue above and below the site of section are omitted for purpose of clarity.

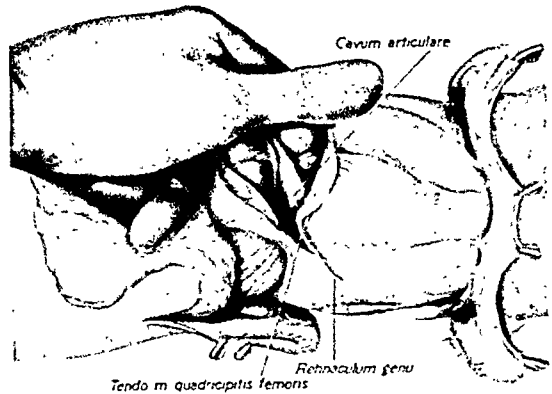


Fig. 6. Section of tendon of the musculus quadriceps femoris. Entry into bursa suprapatellaris genu. Section of retinaculum genu. The suprapatellar bursa of the knee joint has been exposed by an incision through the quadriceps tendon. The fingers are shown inserted into the knee joint to facilitate section of the retinaculum.

The anterior flap is held cephalad and a curved incision is made close to and parallel with the superior border of the patella, in the midline passing through the thick tendon of the musculus quadriceps femoris into the suprapatellar bursa. The knee joint is thus entered. As the incision curves laterally the tendinous attachment of the iliotibial tract is divided. Two fingers are then inserted into the knee joint through the suprapatellar bursa, first on one aspect, then on the other; the retinaculum genu is lifted up and cut

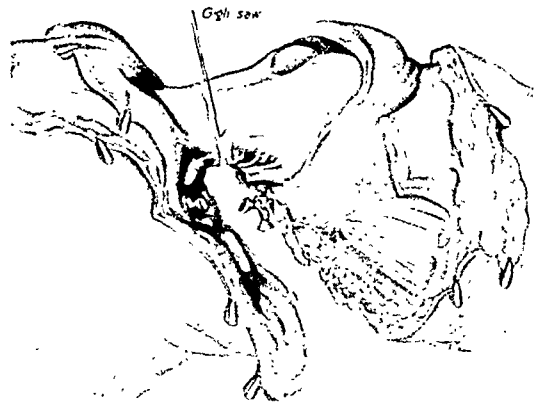


Fig. 8. Amputation is performed throughout the medullary portion of the bone about 2 centimeters above the adductor tubercle. The gauze tapes which protect the soft tissue from bone dust are purposely omitted from the drawing.

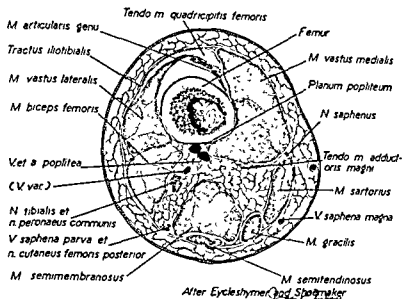


Fig 9 Cross section at the site of amputation showing the somewhat rounded femur. The proximity of the popliteal vessels to the posterior surface of the femur is apparent. The nerve is shown lying posterior and lateral to the vessels.

over the space between the separated fingers as shown in Figure 6. The medial retinaculum must be sectioned more distally than the lateral retinaculum to avoid the low-lying muscular fibers of the vastus medialis. The surgeon then sections the tendon of musculus adductor magnus or its lower musculotendinous attachments to the femur

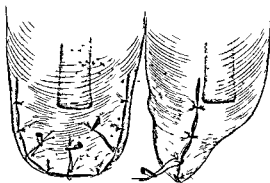


Fig 10 Appearance of stump at conclusion of operation. Closure is effected by approximating skin and subcutaneous tissue only. Interrupted silk sutures are placed at about 3 centimeter intervals. The first 2 sutures adjoining the proximal limit of the suture line are tied in the usual manner. The rest of the stump is closed by tying every other stitch. The untied stitches have a single loose knot. After drainage has completely stopped these are tied.

up to the level of the proposed section of the femur (Fig 7). This procedure divides the last remaining tissue below the site of amputation except the bone, the synovia of the knee joint, and the areolar tissue immediately surrounding it.

*Section of the bone and treatment of the bone end.* Until recently artificial legs were usually suspended from shoulder straps, and the retention of the beginning condylar flare was a great aid in anchoring the stump well down in the socket of the prosthesis. More recently, however, improved ischial supports have eliminated the tendency of the stump to leave the socket and have allowed us to cut the bone at a slightly higher level where it is more round or oval. This site is usually about 2 centimeters above the adductor tubercle. Although it is through the medullary portion of the femur, the ability to bear the body weight directly on the end of the healed stump is in no way impaired. This produces a conical stump which contains no protuberances to act as favorite sites for the development of pressure sores. The removal of an additional three quarters of an inch of bone length is of no importance in such a low amputation.

The sectioned tissues of the thigh and leg are now completely covered with warm, moist tapes, and the lower femur is left free. The site having been selected it is marked by a circular incision

through synovia, areolar tissue, and periosteum, all of which are freed from the bone with periosteal elevator for about 0.5 centimeter. In amputation for vascular disease denudation of the bone is avoided as much as possible. The tendency to strip the muscles from the bone should be carefully restrained. The bone is then sectioned with Gigli saw in a direction perpendicular to the long axis of the thigh (Fig. 8). Special care is necessary to keep the saw in the desired plane. The second assistant steadies the leg and knee as the surgeon slows down to saw through the last portion of the bone to prevent fracture of the stump. The leg is then removed. The edges of the bone end are rounded with a coarse file. If bleeding occurs from the marrow it should be carefully controlled by pressure or bone wax. Failure to do so has caused hematoma of the stump which resulted in delayed healing. The tapes, now contaminated with bone dust, are removed.

*Irrigation, hemostasis, and closure.* The entire stump is now thoroughly irrigated with warm salt solution. Scrupulous care is exercised to ligate every bleeding point. The tendency to oozing is considerable because of the lack of tension in the closure. As the flaps are inspected they are found to be quite loose, extending 2 to 4 centimeters past the bone end (Fig. 10). They should not be trimmed. The closure consists only in approximating the skin and subcutaneous tissues with interrupted sutures of No. 1 silk about 2 inches apart. Between these, additional sutures are placed and loosely tied with one knot. A dressing is applied to the stump which gives even and firm

pressure and which tends to draw the suture line posteriorly. Special care is taken to obliterate the posterior space by an extra pressure pad. The whole stump is wrapped in oiled silk so that the lower end is free for ventilation. The protection is advisable in order to prevent contamination from urine.

In a few cases the closure was modified by making a 2 inch incision in the center of the posterior flap for drainage and by completely closing the skin incision. The drainage opening did not function well and allowed serum and blood to accumulate in the stump. It was therefore abandoned. The author finds the method detailed more satisfactory.

*Postoperative course.* The patient is placed in a bed fitted with a Balkan frame and hand trapeze. He is encouraged to move the stump as soon as possible. The stump is allowed to rest horizontally; it is not elevated lest flexion contracture result. For about 3 to 4 days it is normal for the stump to drain a large amount of serum. Dressing is done on the third day. Only when the discharge of serum has ceased are the sutures previously placed tied. At the first dressing it will be noted that the skin has contracted so as to fit more or less snugly about the bone end, and the hamstrings have drawn the suture line well posteriorly. Sutures are removed on the tenth or twelfth postoperative day.

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# CYCLIC CHANGES IN THE MAMMARY GLAND OF THE RHESUS MONKEY

## Preliminary Report

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SINCE the classical demonstration by Hirschmann and Adler (1908) of histological alterations in the human endometrium during the menstrual cycle, similar rhythmic changes have been sought in other portions of the reproductive tract. In addition to the numerous local and systemic physiological and biochemical changes which have been correlated with the bleeding cycle (Ehrenfest, 1937), structural alterations of a cyclic nature have also been described in the mucosa of the fallopian tube (Snyder, 1924), cervix (Wollner, 1937), and vagina (Dierks, 1927).

A large and controversial literature has arisen concerning the existence and nature of changes in the human breast in relation to the menstrual cycle. It has long been known that many women experience a sense of fullness and an increase in the size of their breasts before the onset of each menstrual flow. This well established phenomenon has recently been demonstrated in a more or less quantitative fashion Reimann and Seabold (1933) measured the areas of x-ray silhouettes of the breasts of women at various stages of their cycles and found a premenstrual increase in size, with a decrease during the postmenstruum Geschickter (unpublished), with the aid of an ingenious funnel-shaped apparatus, has been able to demonstrate volumetrically an increase in breast size antedating the onset of menstruation, with a corresponding postmenstrual decrease.

The first attack upon the problem of the histological changes during the cycle was the report of Rosenberg (1922). On the basis of his study of breasts obtained at autopsy he constructed a very definite cycle for the human mammary gland. This consisted of a premenstrual proliferation and budding of the ducts, with canalization of the buds at menstruation. During the postmenstrual period regression occurred, so that by day 10 of the cycle the lobules had completely disappeared and only the ducts remained. Polano (1924) made a study of human biopsy specimens and agreed in principle with Rosenberg but found wide indi-

vidual variations in the degree of postmenstrual regression, which prevented him from regarding the cycle as so definite and striking a phenomenon as had Rosenberg. Ernst (1925), Berberich and Jaffé (1925), and Sebenius (1925) also accepted, with minor modifications, Rosenberg's idea of the cycle, each author basing his conclusions upon histological study of autopsy material.

Dieckmann (1925) criticized severely the interpretations of Rosenberg and found it possible to rearrange the latter's cases so that the histological picture of each could be correlated with the age of the patient rather than with the menstrual cycle. Dieckmann regarded the lobular development seen in some specimens as due to the greater age of the patient, and strongly objected to the idea of a postmenstrual regression of the lobules. He did, however, describe a premenstrual lobular swelling or "Lappchenodem," with subsequent shrinkage of the lobule during the interval. Moszkowicz (1926) examined a series of biopsy specimens obtained at operation for various types of mammary disease and confirmed the premenstrual edema of Dieckmann, describing in addition a premenstrual infiltration of round cells in the lobules with regression during the interval. Subsequent writings have done little to clarify the situation. Luchsinger (1927), for example, confirmed the findings of Rosenberg but was able to find the lobular edema of Dieckmann only in exceptional cases, while Kueckens (1929), after examining sections from more than a hundred human glands of various ages, found no definite cycle of any type. More recently Lewis and Geschickter (1934) expressed agreement with the composite ideas of Rosenberg, Dieckmann, and Moszkowicz, describing cyclic changes in the parenchymal elements and in the degree of lobular edema and of cellular infiltration. Ingleby (1932) had even made the statement that "premenstrual proliferation is much more rapid than carcinomatous growth." Taylor (1936), however, after reviewing the literature and on the basis of his own studies, was unable to accept the theory of a parenchymal cycle, although he did observe cyclic changes in the stroma. Friedman, Finkler,

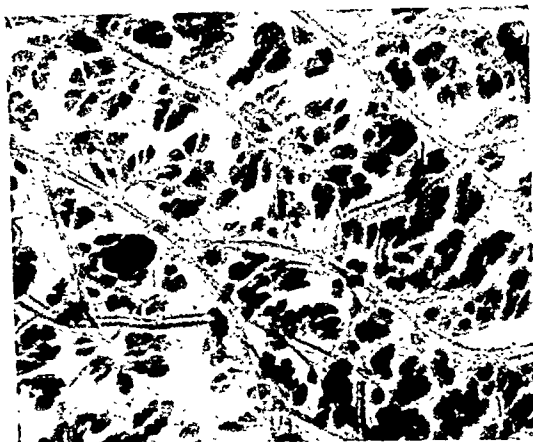


Fig. 1. Biopsy specimen of monkey mammary gland at day 22 of cycle, 11 days after the occurrence of ovulation. Whole mount; alum cochineal.  $\times 7.5$ .

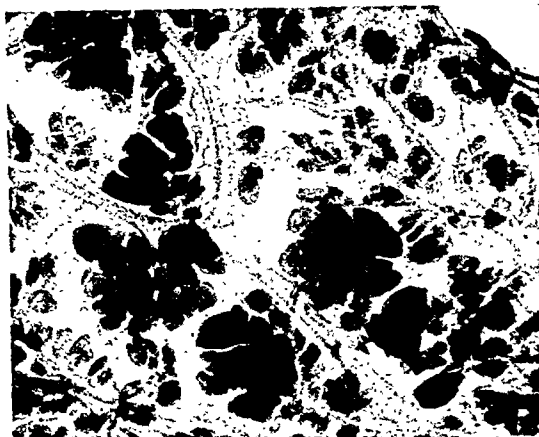


Fig. 2. Mammary biopsy specimen, same animal 5 days later, showing lobular enlargement during premenstruum of ovulatory cycle. Whole mount; alum cochineal.  $\times 7.5$ .

and Antopol (1939) likewise were unable consistently to correlate the histological pictures of 45 biopsy specimens with the specific stages of the menstrual cycle.

In addition to these claims for, and denials of, cyclic changes in the histology of the human mammary gland, Pallot (1935) has reported an increase in the height of the epithelial cells during the premenstruum and a concomitant swelling of the myoepithelial cells, and Grynfeldt (1938) has described the appearance of lipid granules in the alveolar cells during the same period.

In summary, cyclic changes have been described in the human mammary gland with respect to epithelial proliferation and lobular growth, the size of the epithelial cells, the lipid granules within the cells, and the degree of edema and of cellular infiltration within the stroma. Because of the marked disagreement in the literature with respect to the existence and extent of the various cyclic changes described, the status of the problem is unsatisfactory at present.

There are several difficulties, some seemingly insuperable, incumbent upon attempts at settling the question of a cycle in the human mammary gland. Due to the conical shape of the human breast and its large quantities of fat and connective tissue, the mammary gland can be studied only in histological section and is not adaptable to study in whole mounts, as is possible in many laboratory mammals. Thus a gross view of the lobules and their arrangement cannot be obtained. Because of the necessary reliance upon histological sections, only limited portions of the gland can be examined, and it is generally accepted that marked variations may exist simultaneously in

different parts of the same human breast. In most studies, furthermore, attempts have been made to compare the glands of different women, thereby introducing the additional complicating factor of individual variation. Of great importance is the fact that practically all studies have been based upon the examination of mammary tissue the normalcy of which may be seriously questioned; that is, tissue obtained at autopsy after death from a variety of causes, or biopsy specimens from breasts which were being operated upon for pre-existing mammary pathology, such as neoplastic or cystic disease. Moreover, in most instances only the day of the menstrual cycle was known, and rarely was this correlated with studies of sections of the endometrium. The occurrence and relative frequency of anovulatory menstrual cycles in the human is becoming more generally recognized, and it will therefore be evident that in the absence of endometrial biopsy or urinary pregnandiol assays, essential data are lacking for the proper interpretation of cyclic changes in the mammary gland. For without such information one has no knowledge of the presence or absence of a functional corpus luteum, an organ of great importance in mammary physiology.

The question of a mammary cycle has not been investigated in subhuman primates. The rhesus monkey would appear to be the ideal animal from which to obtain evidence of possible applicability to the human; for in addition to the similarities in the menstrual cycle and the reproductive physiology of the two species, the macaque mammary gland is subject to none of the objections which have been raised against the interpretation of human material. Whole mounts can readily be



made of the monkey mammary apparatus, either of the whole gland or of biopsy specimens; and since the gland of the intact animal is, as a rule, quite uniform in structure, as has been found in an examination of more than 200 pairs of mammary glands, a specimen of sufficient size may be considered as representative of the entire gland. By using rhesus monkeys one can perform repeated biopsies upon the same animal, free of mammary pathology and accurately dated with respect to the menstrual cycle. In addition it has been possible to ascertain and time the occurrence of ovulation during the cycle, by means of recto-abdominal palpation (performed by Dr. Carl G. Hartman).

Nine monkeys having regular menstrual cycles were studied by biopsies performed on alternate breasts at intervals of about one week. Daily vaginal lavages were made to determine the onset of menstruation, and bimanual palpation for the ascertainment of ovulation. In addition several laparotomies were performed to check the diagnosis of ovulation. Thirty-nine biopsies, covering 7 ovulatory and 6 anovulatory cycles, were studied by means of whole mounts and histological sections.

From examination of the whole mounts it is possible to establish the existence of a definite series of cyclic mammary changes which bear a fixed temporal relation to the menstrual cycle. Beginning 7 to 10 days before the onset of the menstrual flow the lobules begin to enlarge, and in some instances the individual acini appear to dilate. Premenstrual lobular swelling has been observed to occur with varying rapidity, in some cases definite changes were found in specimens removed a few days apart. Figure 1 is the whole mount of a biopsy specimen obtained on day 22 of the cycle, 11 days after ovulation. Figure 2 is a mammary specimen, at the same magnification, taken from the same animal 5 days later. Since hysterectomy was performed at the time of the first biopsy, for purposes of another study, menstruation did not set in at the expected time. The enlargement of the lobules is readily apparent.

These changes attain their height at about the time of menstruation and slowly regress during the postmenstrual period and interval. They have been found, however, only in those cycles in which ovulation has occurred. In anovulatory cycles, no lobular enlargement has been observed, and little if any change can be detected during the premenstruum.

Study of the histological sections has confirmed, in general, the changes noted in the mounts. En-

largement of the acini was seen soon after ovulation and persisted throughout the premenstrual period, gradually subsiding during the early part of the next cycle. This premenstrual enlargement of the acini was not found among the anovulatory cycles. Another rather striking contrast between the ovulatory and anovulatory cycles was found in the degree of vascularity of the lobules. During the premenstrual stage of a cycle in which ovulation had occurred, many widely dilated capillaries, filled with red blood cells, were seen in the interacinar spaces. Little if any vascular changes could be detected during anovulatory cycles. No definite changes could be made out regarding the degree of cellular infiltration of the lobules at different stages of the cycle.

In summary, a cycle, dependent upon the occurrence of ovulation, has been established for the mammary gland of the rhesus monkey. The striking features of the cyclic changes are the enlargement and the increase in vascularity of the lobules and the dilatation of the acini during the premenstrual and menstrual periods.

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# POSTPARTUM PYELOURETERAL CHANGES FOLLOWING HORMONE ADMINISTRATION

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**C**ONSIDERABLE divergence of opinion exists concerning the etiology of ureteral dilatation during pregnancy.

The study of the urinary passages in pregnancy has been greatly facilitated by the discovery of radio-opaque substances, by means of which the urinary tract can be visualized directly on the x-ray plate. Kretschmer, Heaney, and Ockerley (19, 20), Lee and Mengert (22, 25), Dugald Baird, Duncan and Seng, and numerous other workers, by means of intravenous and retrograde pyelograms, found some degree of dilatation of the upper urinary tract in every pregnancy—100 per cent on the right side and 85 per cent on the left. The earliest attempt at explaining so universal a change occurring during normal pregnancy was made by Opitz in 1905. He believed that the dilatation of the ureters during pregnancy was caused by pressure of an enlarging uterus on the ureters. Baird performed autopsies upon 102 women, who died during pregnancy or within a few days of delivery, and found that the right ureter in the later months of pregnancy was frequently compressed between the uterus and the psoas muscle or the common iliac artery on that side. The left ureter was afforded some degree of protection by the more posterior position of the common iliac artery and because the ureter follows a more or less parallel course to that vessel rather than crossing it at right angles. Further protection was afforded by the promontory of the sacrum and the cushion-like effect of the sigmoid colon. Similar observations have been made by Carson, Hundley, and others. In quadrupeds this pressure factor, for the most part, is low (Crabtree). Mengert (24), after a study of pregnancy in the cow, rabbit, guinea pig, rat, hog, and monkey, concluded that the ureters of these animals did not dilate during pregnancy. However, dilatation of the ureters has been recorded during pregnancy in animals, and these changes are recognized in veterinary medicine. Dilatation of the ureters has been observed in the rabbit by Rossi, and in the monkey by Van Wagenen and Jenkins.

Baker and Lewis studied 16 cases of ovarian cysts and fibroid uteri, all larger than the size of a 3 months' pregnancy, by means of intravenous pyelograms. They found bilateral ureteral dilatation in 63 per cent, and right sided dilatation alone in 37 per cent of the series. Dilatation of the urinary tract was found to disappear with the removal of the tumor in all cases. Similarly, Kretschmer and Kanter (21) found changes in the urinary tract in 64.7 per cent of gynecological disorders, including fibroids, ovarian cysts, and prolapse of the uterus. Following surgery, 72.5 per cent of these cases return to normal.

From studies of frozen sections of pregnant women at term, Hofbauer (16, 17) concludes that the probability of ureteral pressure as an etiological factor in causing ureteral dilatation has been shown to be untenable. In a complete histological study of the urinary tract at various levels, Hofbauer found both hypertrophic and hyperplastic changes in the musculature and connective tissue of the pelvic portion of the ureter. These changes histologically resemble those occurring in the lower uterine segment during pregnancy. A striking feature of Hofbauer's study was the finding of excessive hypertrophy of the external longitudinal ureteral sheath of Waldeyer.

Traut, McLane, and Kuder (27, 28, 29), in a series of experiments, described a progressive decrease in peristaltic activity and tone of the ureters as pregnancy advanced, up to the seventh month, after which time a definite return of muscular irritability was observed. By means of intravenous pyelograms, they found that the degree of ureteral dilatation is proportional to the diminution of ureteral activity. Following close on the returning irritability of the ureteral musculature, dilatation was found to be less marked as term approached. They believe this loss of tone and irritability to be contributory to the dilatation of the ureters, i.e., atony is primary, with dilatation a secondary development, the whole process being affected in varying degree by the weight and torsion of the pregnant uterus. Traut and McLane suggest that the etiology of ureteral atony, hence, ureteral dilatation, may be chemical.

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The mechanical pressure theory cannot adequately explain the diminution of ureteral dilatation during the last weeks of pregnancy when the uterus is approaching its maximum size.

The observations here noted are suggestive of other factors apart from obstruction, which influence the behavior of the ureters during pregnancy.

In the past few years various European and American workers have studied the influence of various hormones on ureteral contractility, irritability, and dilatation.

Bompiani, working with isolated animal ureters kept alive *in vitro*, demonstrated increased peristalsis of the ureter with human pregnancy urine of the second month and a marked decrease of motility with pregnancy urine of the eighth month. Corpus luteum and folliculin were found to inhibit peristalsis, whereas gonadotropic hormone increased motility. Grossu-Streja and Georgesco, using isolated pig ureters, also obtained inhibition to ureteral peristalsis by the use of folliculin and corpus luteum hormones, but, unlike Bompiani, observed inhibition also with gonadotropic hormone. Contiades, Villaret (9, 10, 31, 32), and their co-workers found inhibition of ureteral muscular activity of isolated dog and cow ureters with folliculin, corpus luteum hormone, amniotic fluid, and term urine which had been boiled in order to destroy its prolactin content. They also mention 2 cases of pregnancy with diabetes insipidus in which the urine caused decreased rhythm of contraction, the action of which strongly resembled that of folliculin. Further, they found that both anterior and posterior pituitary extracts caused acceleration of peristaltic activity.

Rossi, by means of intravenous pyelograms, found that the appearance of the best plates in pregnant rabbits near term is obtained 15 to 20 minutes after injection of the dye, while in the adult, nonpregnant rabbit the best plates were obtained in 3 to 4 minutes. Interestingly enough, he also reports a less marked dilatation of the ureter just before delivery. Rossi injected serum from the blood of pregnant rabbits near term into nonpregnant female rabbits and obtained delayed maximum visualization of the urinary tract up to from 15 to 20 minutes. He also found a progressive increase in ureteral dilatation in these animals up to 72 hours, after which time regression of these changes occurred. Crabtree, Abramson, and Robins confirmed the finding of Rossi of delayed appearance of the best plates in pregnant rabbits after intravenous injection of diodrast.

Brack and Langworthy (4, 5), who demonstrated an increased vesical capacity in rabbits during pregnancy, showed a similar increase in 50 per cent of their cases 10 days after injection of antuitrin S intravenously. They also found a slight decreased vesical capacity 1 week after injecting progynon B, followed in 2 to 3 weeks after injection by an increase in average capacity.

After the prolonged administration of estrogenic hormone in both male and female mice, Burrows found dilatation of the urinary bladder and ureters with hydronephrosis, sometimes accompanied by a purulent cystitis and pyelitis.

Draper, Darley, and Harvey reduced the size and density of pelvic and ureteral shadows, as shown by intravenous pyelograms, by intramuscular injections of pituitary extract and pitressin.

Dugald Baird found that in cases of toxemia the amount of ureteral dilatation was consistently slight. This observation he interpreted to be the result of a probable overproduction of posterior pituitary hormone in toxemia, thus accounting for the lack of atony.

Van Wagenen and Jenkins, in a study of factors causing ureteral dilatation in pregnancy, attempted to remove the mechanical factor by removing the fetuses of pregnant monkeys by cesarean section in various periods of gestation. The hormonal relationships were preserved by leaving the placenta undisturbed in the uterus. They found that dilatation of the upper urinary tract can develop after removal of the fetus while the placenta remains in a functional state within the uterus. This dilatation disappeared only after the placenta separated and was delivered spontaneously at the end of a period of time which corresponded to the end of the normal period of gestation in the monkey.

In view of the reports presented we were of the opinion that additional information could be gained by analyzing the effects of various hormones upon the postpartum ureter. This physiological dilatation of the genitourinary tract regresses fairly rapidly to normal in the postpartum period. Kretschmer and Heaney (19), Ockerley (20), and Hundley and his co-workers found that 96 per cent of their cases regressed to normal by the sixth week postpartum. Lee and Mengert, and Duncan and Seng state that a majority of their cases regressed to normal by the ninth postpartum day.

In a series of 10 cases McConnell and Gray found 2 cases returned to normal, there was a reduction of dilatation in 2 cases, while in 2 others there was a very definite increase in dilatation in a period of less than 10 days postpartum.

With these results as a guide, we believed that any consistent deviation in the rate of involution of the postpartum ureter in a group receiving a hormone preparation might possibly be caused by the specific effects of the hormone administered. In the postpartum period the kidney pelvis and ureter can easily be visualized, and it was believed that this was a safe period in which to administer the various hormone preparations used, some of them in fairly large doses.

#### METHOD

All the cases studied in this series were selected. The patients were all primiparous. In no patient was there any history of previous genito-urinary disease. The antepartum urine examinations were all negative for albumin and white blood cells. None of the patients had signs or symptoms of toxemia of pregnancy, nor did any of them have hypertension. The ages varied from 17 to 28 years. Only patients who had spontaneous or outlet forceps deliveries were included. Intravenous pyelograms after the administration of 20 cubic centimeters of diodrast were taken in all cases during the first 24 hours after delivery, 7 days postpartum, and, lastly, as close to the 6 week postpartum period as was possible in those patients who returned for follow-up.

In this series 30 patients were studied; they were divided into 5 groups of 6 patients each, in the following order:

The first group was used as controls, no hormone being administered.

The second group was given 1 cubic centimeter (10 international units) of posterior pituitary extract intramuscularly, daily for 7 days.

The third group received 1 milligram (1 international unit) of progesterin in oil intramuscularly, daily for a period of 7 days.

The fourth group was given 1,000 rat units of anterior pituitary-like hormone daily for 7 days, subcutaneously.

The fifth group received 5 milligrams of stilbestrol orally, daily for a period of 7 days.

The hormones mentioned were administered during the first 7 days postpartum, in the interval between the first and seventh day pyelograms.

#### SIDE EFFECTS

A total of 75 pyelograms were taken with no harmful effects, aside from mild nausea in an occasional patient. In the patients who were given stilbestrol there was a definite diminution in the amount of lactation in 4, and in 2 the breasts dried up completely by the fifth postpartum day.

Marked acne of the face improved remarkably in 1 patient who was given stilbestrol. However, the acne was again marked when the patient was seen 6 weeks postpartum, during which time she had not received stilbestrol. No changes in involution of the uterus were noted in the groups treated with stilbestrol and anterior pituitary-like hormone. In the group of 4 patients who were given progesterin there was definitely slow involution of the uterus, and in this group was the only patient in the entire series who developed a low-grade endometritis.

#### RESULTS

In the series of 30 patients studied within 24 hours following delivery, some degree of dilatation of either the kidney pelvis or the ureter was observed in 30, or 100 per cent, of the patients. Dilatation was noted on the right side in 29, or 96.6 per cent, and on the left side in 14, or 46 per cent. The right side alone was involved in 16, or 53 per cent, and the left side in 1, or 3.3 per cent. In the repeat pyelograms on the seventh day postpartum, 9, or 30 per cent, of the patients who previously had had some slight, moderate, or marked degree of dilatation of the kidney pelvis or ureter had already returned to normal. Four, or 13.3 per cent, revealed pronounced regressive changes, with the ureter and pelvis almost approaching the normal. Six, or 20 per cent, revealed moderate to slight regressive changes; all these patients showed some degree of improvement in appearance of the pelvis and ureter over that of the first plate. Eleven, or 36.6 per cent, showed either no changes or a slight degree of increased dilatation of the ureter or kidney pelvis. Only 13 of the patients in this series returned at the end of 6 weeks for a final pyelogram, and all these were found to have normal appearing plates.

#### CONTROL GROUP

In this group 2 patients returned to normal within 1 week. One of these patients had moderate ureteral and pelvic dilatation on the right side, and the other a marked degree of ureteral and pelvic dilatation with moderate hydro-nephrotic changes, also on the right side. In 3 patients no changes were found at the end of 1 week. One of these had a bifid ureter and pelvis on the right side and developed a postpartum pyelitis on the fourth day which persisted up to the seventh day. At the end of 6 weeks this patient had a normal pyelogram. In this group there was 1 patient who showed moderate regressive changes on the seventh day.

## POSTERIOR PITUITARY

The group of patients who received posterior pituitary extract revealed the most striking results in the entire series. In these 6 patients pyelograms were completely normal in 4 on the seventh day, and in the other 2 patients—both of whom had marked ureteral and hydronephrotic changes—pyelograms were almost normal in appearance except for slight dilatation of the renal pelvis.

One patient in this group developed a bilateral postpartum pyelitis on the second day which lasted until the seventh day. This patient had chills, fever, (temperature 104.2 degrees), some pain in the back, dysuria, and a moderate degree of bilateral costovertebral tenderness. Examination of the urine disclosed 2 plus albumin and numerous white blood cells, singly and in clumps. Pyelograms of this patient on the seventh day and 6 weeks postpartum were entirely normal.

## PROGESTIN

The results obtained in this group were also impressive, but in an opposite direction. Pyelograms of 5 of these 6 patients at the time the second plate was taken revealed either no changes at all or some increased dilatation of the kidney pelvis and ureter on one or both sides. In 3 patients there was slow involution of the uterus, and in 1 patient slow involution with a mild endometritis (temperature 100.6 degrees on the sixth day, and 101 degrees on the seventh day). In only 1 patient of the entire group were there evidences of a regressive nature. In none of these patients was the pyelogram normal on the seventh day. One patient had a normal pyelogram in the sixth week postpartum.

## ANTERIOR PITUITARY-LIKE HORMONE

A study of the seventy day plates of this group demonstrated that the ureters and kidney pelvis more closely approached the normal than did those in the nonmedicated group. Two patients with moderate dilatation of the ureters and kidney pelvis during the first 24 hours were found to have a normal appearing genito-urinary tract on the seventh day postpartum. Two patients showed marked regressive changes on the seventh day. One of these developed a left pyelitis on the sixth day. Pyelograms of this patient on the seventh day disclosed a normal kidney pelvis and ureter on the right side and slight regressive changes on the left side. One patient showed no changes in the appearance of the urinary tract during the first week, while another showed mod-

erate regressive changes on the seventh day. Pyelograms of both these patients were normal 6 weeks postpartum.

## STILBESTROL

The results obtained in this group were similar to those in the group that received no medication. In 1 patient with marked dilatation of the pelvis and ureter on the right side there was normal involution by the seventh day. In 3 patients there were slight to moderate regressive changes, and 2 showed no changes on the seventh postpartum day. Three of the last 5 patients had normal appearing urinary tracts 6 weeks postpartum.

## EVALUATION

The incidence of ureteral and pelvic dilatation at 7 days and 6 weeks postpartum in the series herein reported compares favorably with results published previously, some of which are quoted here. In a period of 7 days following delivery, almost half (43.3 per cent) of the pyelograms were either normal or almost so (showing marked regressive changes), while 56.6 per cent showed slight regressive changes or no change at all. Of the patients who received no medication, 33.3 per cent returned to normal in 1 week. The remainder presented slight or no changes whatever. In the group that received posterior pituitary extract, 100 per cent of the patients returned to normal, or almost normal, on the seventh day. In none of the patients who were given progesterin was there a return to normal pyeloureteral involution, nor did any of these show marked improvement during the time that they were receiving the hormone. Four patients in this group showed an increase in the size of the pelvic and ureteral shadows on the seventh day. In the anterior pituitary-like hormone group favorable changes were noted in 66.6 per cent, this being better than for the entire series and for the control group. No significant trend was observed for the stilbestrol group.

The number of patients studied in this series is small, therefore, care must be used in the interpretation of the results obtained. Fairly consistent results followed administration of posterior pituitary extract, in hastening return of ureteral tone, whereas progesterin almost universally delayed this process or caused increased atony.

One might attempt at this point to associate the action of progesterin on ureteral muscle, with its inhibitory action on uterine muscle. However, the physiological antagonist of progesterin, namely

estrin, did not similarly exert its motility-stimulating action on the ureteral muscle, as it does on uterine muscle. A less marked effect was that of the anterior pituitary-like hormone in causing increased regressive changes. These results closely parallel those obtained by Bompiani in his animal experimentations. It might be interesting to view these results with our knowledge of hormonal relationships obtaining during the various phases of pregnancy, and the changes occurring in the genito-urinary tract during these periods of time. One might speculate on the rôle of the increasing concentration of progesterin as pregnancy advances. The slight regression that occurs during the last 2 months of pregnancy might possibly be explained by a secondary rise in the prolactin level, as demonstrated by Browne, Henry, and Venning in a number of patients during the last months of pregnancy.

#### SUMMARY

In this series 30 patients were studied postpartum in an attempt to determine the possible hormonal effects, if any, upon pyeloureteral dilatation. Accelerated return of pyeloureteral dilatation toward the normal was demonstrated following the use of posterior pituitary hormone. To a lesser degree, a similar change was noted following the use of anterior pituitary-like hormone on postpartum pyeloureteral dilatation. The results of stilbestrol administration paralleled an untreated control group. The administration of progesterin was productive of very slight regression in only 1 patient, and in some instances it appeared to increase pyelo-ureteral dilatation.

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## AIRPLANE TRANSPORTATION OF PATIENTS

THE advantages of transporting patients in aircraft are: (1) speed and relatively short duration of flight, (2) comfort and (3) constant attendance by stewardesses who are registered nurses. The chance for recovery is improved greatly by shortening materially the time needed to bring seriously ill patients to their ultimate destination, especially if a major surgical procedure is necessary. Disadvantages of transportation by airplane are adverse weather and the necessity of good airports at the beginning and end of the flight. Transportation of patients by airplane has few absolute contraindications.

The modern commercial airplane is quiet, comfortable, heated, and has adjustable seats or berths. Well equipped medical kits as well as efficient means of administering oxygen, such as the B.L.B.<sup>1</sup>,<sup>2</sup> inhalation apparatus, are essential to planes transporting patients.

The onset of anoxemia among normal persons occurs at an altitude of 10,000 to 11,000 feet, therefore, it is obvious that any clinical condition which causes anoxemia, such as pneumonia, certain types of cardiac disease, fulminating infection, surgical or traumatic shock and so forth, will be borne less well at high altitudes than at sea level unless oxygen is given. Moon has emphasized the damaging effect of anoxia in the perpetuation of shock.

In considering transportation of anemic patients by airplane, it is important to remember that as the arterial blood leaves the lungs, it is normally saturated with oxygen; in cases of anemia, however, less oxygen can be carried as there is a subnormal quantity of hemoglobin with which it can unite. An anemic patient may not be cyanotic when anoxia occurs because cyanosis is a direct result of the amount of reduced hemoglobin present. Patients who have severe anemia should be given oxygen at relatively low altitudes as a prophylactic measure to prevent anoxia.

Schnedorf, Munslow, Crawford, and McClure demonstrated that concussion of the brain, with or without fracture of the skull, caused a decrease in the oxygen content of the arterial blood, and they advised oxygen therapy as a general procedure for such types of injury. Therefore, it seems advisable to administer oxygen to such patients who are being transported in airplanes. There is a slight rise in the pressure of spinal fluid among normal subjects on ascent to the high altitude of 28,000 feet, as demonstrated by Walsh and Boothby. This might result in an aggravation of symptoms in cases of certain types of intracranial

<sup>1</sup>Boothby, Lovelace, Uthleis. *Proc. Staff Meet. Mayo Clin.*, 1940, 15: 104.

<sup>2</sup>Boothby, Mayo, Lovelace. *J. Am. M. Ass.*, 1938, 113: 477.  
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tion. Occasionally an expert endoscopist can pass a long proctosigmoidoscope into the proximal sigmoid and rarely into the lower portion of the descending colon. For all practical purposes, however, that portion of the colon proximal to the midsigmoid cannot be seen directly, but lends itself readily to roentgenological study. Furthermore, the roentgenologist cannot study the rectum to his own satisfaction, and he frequently has difficulty with the rectosigmoid, as the terminal bowel is surrounded by a bony cage. Accordingly, therefore, proctoscopic examination must not be weighed against x-ray studies or some other means of investigation. Rather the several methods should be considered as integral parts of a thorough study of the colon.

The failure to use proctoscopy as a diagnostic procedure is one of the chief factors in a bad end-result. The two chief causes of failure in treating rectal disease, however, are tardiness on the part of the usual patient to report rectal troubles to his doctor, and the failure of the physician when a patient does seek advice to subject the patient to a complete proctoscopic examination. Thus it appears that both the public and the doctor must be further educated.

With regard to the education of the medical student, it must be pointed out that one great obstacle is the astonishing indifference of the medical faculties of many leading schools toward proctology, they are too easily satisfied with a "rectal clinic" devoted to clipping of skin tags and to the injection therapy of hemorrhoids. Medical educators could render great service to the proctologist by encouraging him to teach the medical student the importance of the use of the examining finger and of the proctoscope in his everyday practice.

One great difficulty lies in the actual teaching of the use of the proctoscope. The exam-

iner can instruct students, house officers, and visiting physicians verbally and by allowing each one an occasional look through the proctoscope. He cannot, however, show each observer all the important things to be seen in a given case, nor can he allow each one to pass the proctoscope in this one patient, for to do so would necessitate an undue prolongation of the examination. In a large clinic, over a long period of time, however, duly assigned residents or "fellows" can be properly trained. Unfortunately, such clinics are few, and the number of students or fellows that can be accommodated on the proctologic service is small.

The rôle of color photography in visual education today is well established. Proctoscopic color photography has been delayed because of two problems: one, the provision of sufficient light, and the other, the absolute necessity of maintaining direct vision at all times to avoid any possibility of injury to the bowel. The apparatus designed by Garner with the aid of his technical adviser, Brubaker, answers the most rigid requirements of safety for the patient, and its use adds but little to the time required for a routine proctoscopic examination. The pictures enable the observer to see on the screen exactly what the examiner sees through the proctoscope.

Thus color photography has paved the way toward easier teaching and study of proctoscopy. Such pictures should serve well in the education of the medical student. They should enable us to bring to the general practitioner an accurate conception of the possibilities offered by proctoscopy in both the prevention and the early diagnosis of rectal and colonic disease. For this contribution proctologists especially, and the profession in general, should be grateful.

J. PEERMAN NISSELROD.

# CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

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## PRELIMINARY PROGRAM FOR 1941 CLINICAL CONGRESS

THE thirty-first annual Clinical Congress of the American College of Surgeons will be held in Boston November 3 to 7, when the fellows of that great medical center will sponsor a clinical program of unusual interest. The operative clinics and demonstrations which are to be held in the hospitals will cover many phases of general surgery and the surgical specialties. Leaders of the profession from many sections of the country will participate in the panel discussions and other scientific meetings at the headquarters hotels. The Hospital Standardization Conference will attract many visitors of outstanding reputation in the hospital field. Each Congress that has been held in Boston—the first in 1915, the last in 1934—has made notable contributions to medicine and surgery. Those who attend in 1941 may anticipate a program of broad scope and interest, for the surgeons and clinicians of Boston have complete facilities at their command in the three medical schools and 30 or more approved hospitals.

### CLINICAL PROGRAM

Under the leadership of a strong and representative Committee on Local Arrangements, the clinical program for the five-day meeting is practically complete. An extensive schedule of clinics, symposia, and demonstrations is being arranged in the hospitals and medical schools which will, as usual, be the major feature of the Congress. Visiting surgeons will be given opportunity to observe and obtain first-hand information on a wide variety of surgical and related subjects, in the favorable environment of excellent hospital facilities. In the operative clinics, surgical technique, use of operating room equipment, and organization of personnel will be demonstrated.

The symposia and non-operative clinics will deal with the broader, but equally important aspects of diagnosis, related medical treatment, pre-operative preparation and postoperative care. The discussions will be augmented by the presentation of clinical material. Diagnostic methods will be demonstrated by various hospital departments. Specialists in many other fields, as well as surgeons, will participate in the clinical program at the hospitals in order that the subjects may receive consideration from different viewpoints. A preliminary clinical program appears on the following pages. Several additional hospitals have been invited to prepare programs which will appear in subsequent publications and the final program.

The medical schools and their affiliated hospitals are developing a series of exhibits presenting their work in clinical investigation and the latest advances in surgical research. These exhibits will be available for study in the local hospitals during the entire meeting. Basic science departments of the medical schools will contribute to the program by arranging exhibits and demonstrations related to surgical practice. Thus the Boston institutions have much to offer in the way of a highly concentrated postgraduate course in surgery and allied subjects.

The schedule of each hospital is arranged to cover subjects in general surgery, obstetrics and gynecology, fractures, orthopedic surgery, thoracic surgery, neurosurgery, genito-urinary surgery, ophthalmology, otorhinolaryngology. Thus the visiting surgeon may readily select the clinics which he wishes to attend. Presentation of subjects under these classifications is so correlated that he will have the opportunity to devote his time continuously to clinics dealing with the spe-

cialty in which he is most interested. The clinical program as published daily will be arranged according to these classifications. Each afternoon during the Congress, the complete detailed clinical program for the succeeding day will be posted in the form of bulletins at headquarters in the Statler Hotel. On the following morning, this final program will be distributed in printed form. As much information as it is possible to obtain in advance is being published in the preliminary programs and the general program, but it is necessary that those who attend the Congress make their clinic ticket selections from the daily bulletins. This will facilitate proper selections and distribution of clinic tickets.

#### SCIENTIFIC SESSIONS

Eminent surgeons and specialists, recognized as authorities in their respective fields, will address the scientific meetings to be held on Tuesday, Wednesday, and Thursday evenings in the ballroom of the Copley-Plaza Hotel. The annual oration on surgery will be given by Dr. W. Edward Gallie, Toronto, Ontario, on Tuesday evening. The Board of Regents of the College has given careful attention to the selection of speakers and subjects for these evening sessions so that a well-rounded program introducing the newer developments in general surgery and the surgical specialties may be assured.

During recent years, at both the Clinical Congress and sectional meetings of the College, panel discussions held at the headquarters hotel each afternoon have been of unusual interest. Therefore, a schedule of thirty-six of these sessions has been planned for Monday, Tuesday, Wednesday, Thursday, and Friday. Recognized authorities in the fields under discussion will lead these panels, and with the aid of collaborators especially qualified, will present the fundamental facts and direct the discussions in such a way that different viewpoints may be expressed. These sessions afford an opportunity for a larger number of surgeons to participate in the discussions and learn of the ideas and experiences of others. The general plan is for the leader to give a ten-minute presentation of the subject, collaborators to follow with brief remarks on different phases of the topic. Then as the major and final feature of each session, general discussion from the floor will be encouraged. This type of program will permit more informal discussion than usually takes place in larger general meetings. The subjects of the panels are carefully selected in order to cover many pertinent problems in various fields of surgery.

Important features of the afternoon meetings at the headquarters hotels are a symposium on "Cancer" on Tuesday and one on "Fractures and Other Traumas" on Wednesday. There will also be special panel discussions on "The Organization and Conduct of Cancer Clinics in Hospitals," and "Graduate Training in Surgery." Because of the wide interest in these subjects, it is expected that these meetings will attract a large attendance.

It is the aim of the Board of Regents and the local committee to provide a type of program that will enable each individual surgeon to learn of the newer developments in his field of practice. The subjects presented in the hospital clinics, panel discussions, and other scientific meetings will appeal to the surgical specialist as well as to the general surgeon. Each feature of the meeting has been carefully planned with this idea in mind. The detailed programs of these sessions will be found on the following pages.

#### PRESIDENTIAL MEETING AND CONVOCATION

The always impressive processional of the officers, regents, and honorary guests will open the combined Presidential Meeting and Convocation to be held in Symphony Hall on Monday evening. Welcome will be extended to the assembly by the chairman of the local Committee on Arrangements, Dr. Leland S. McKittrick. Honorary guests will then be introduced, following which Dr. Everts A. Graham, the retiring president, will deliver the presidential address. Other events on the program of this meeting will be the inaugural ceremony for the incoming officers, the presentation of the initiates for fellowship, and the awarding of the Medical Records Prize.

#### ASSEMBLY OF INITIATES

On Monday afternoon there will be held the Assembly of Initiates. This meeting will be presided over by Dr. Everts A. Graham, and Dr. Albert O. Singleton, Galveston, Texas, Vice-President of the College. Dr. Bowman C. Crowell and Dr. Malcolm T. MacEachern will discuss "The Program of the American College of Surgeons." Initiates will then recite the fellowship pledge and greetings will be extended by Dr. W. Edward Gallie, Toronto, President-Elect of the College. Closing remarks will be made by Dr. Irvin Abell, Chairman of the Board of Regents.

#### FORUM ON FUNDAMENTAL SURGICAL PROBLEMS

As a new feature to be introduced at the Clinical Congress in Boston, the Board of Regents of the College has authorized the holding of a "Forum on Fundamental Surgical Problems." Plans for the

forum have been formulated by a committee under the chairmanship of Dr. Owen H. Wangenstein of Minneapolis. For many years, a great deal of clinical and experimental research has been done by younger surgeons working in medical schools and representative clinics and hospitals. Some of this work has resulted in outstanding contributions to medical and surgical knowledge. The results of much of this work are published but there has been limited opportunity for many of these younger surgeons to express themselves before larger medical groups. Recognizing this fact, it is felt that the American College of Surgeons should encourage the work of these men by providing a place on the program of the Clinical Congress for them. Therefore, the "Forum on Fundamental Surgical Problems" has been organized.

Sessions will be held on Tuesday, Wednesday, and Thursday mornings, with presentations of original and experimental work related to general surgery and the surgical specialties. There will be no prepared discussions but opportunity will be afforded those who attend to ask questions. Presentations will be limited to ten minutes each. Some of the best that is new in surgery will be presented and there is every indication that a live and active surgical forum in which younger men may participate will constitute one of the most important activities of the Congress in the future.

In formulating the preliminary plans for the forum, the committee in charge has been highly pleased with the response to this idea. Over 125 abstracts of subjects available for presentation have been submitted and from this material, the committee will select the most outstanding for the forum. The subjects, together with brief abstracts, will be published in the final general program of the Clinical Congress.

#### OPHTHALMOLOGY AND OTOLARYNGOLOGY

An extensive program of scientific sessions and clinical demonstrations for ophthalmologists and otolaryngologists has been planned. Separate sessions scheduled for Tuesday and Thursday evenings will include papers and symposia on pertinent subjects in these fields. The leaders will direct the discussions in the meetings so as to cover many phases of a general subject in each of the specialties. Those attending will have an opportunity to express their viewpoints. On Wednesday evening, there will be a joint meeting of ophthalmologists and otolaryngologists with a symposium on "Neurosurgery as Related to the Eye and Ear." This type of program promises to attract wider interest than the presentation of formal papers.

Clinics in the Boston hospitals each morning and afternoon for the visiting ophthalmologists and otolaryngologists will demonstrate surgical work of great variety. On Tuesday, Wednesday, and Thursday mornings, in addition to the hospital program, there will be clinical conferences for each group of specialists at the headquarters hotel. These are being arranged so that the leader will briefly survey the field for discussion in a ten-minute period. The larger meeting will then be broken up into small groups limited to 20 and under separate leaders where there will be an opportunity for everyone to ask questions and participate in the discussion. Each visitor will select in advance the smaller group which he wishes to attend. In this manner, the general subject may be reviewed thoroughly and each visitor will benefit by the experiences and different ideas of his colleagues. The morning and evening meetings will be preceded by the showing of selected motion picture films on subjects related to ophthalmology and otolaryngology. The detailed programs of these special meetings appear in the following pages.

#### NATIONAL AND REGIONAL FRACTURE COMMITTEES

The meeting of the National and Regional Fracture Committees, with Dr. Robert H. Kennedy, of New York, chairman of the National Committee, presiding, will be held on Thursday afternoon, when this assembly of surgeons will discuss the activities of the respective groups. Working in co-operation with the American Red Cross, other local organizations and public officials, these committees have exerted great influence in improving methods and facilities for the transportation of the injured. They have also made a concerted effort to improve the treatment of fractures in the hospitals of many communities. Pertinent problems will be discussed at the meeting of these committees.

#### ANNUAL MEETING OF COMMITTEES

The annual meetings of the State and Provincial Judiciary, Credentials, and Executive Committees will be held on Wednesday morning. These committees have an important function to perform in the College. The Credentials Committees and the Committees on Applicants constitute one of the largest and most carefully deliberate accrediting bodies which exist in the medical profession. Through this organization the standards of fellowship are maintained and each fellow of the College has a definite responsibility in this work. All of the members of these committees are urged to attend this important meeting.

## ANNUAL MEETING OF FELLOWS

The annual meetings of the governors and fellows will be held on Thursday afternoon in the ballroom of the Copley-Plaza Hotel. The American College of Surgeons has been a potent force which has not only raised the professional and ethical standards of surgery, but has also promoted good hospitalization and general improvement in the practice of medicine in the United States and Canada. Each individual fellow of the College has a part in this work and may extend its influence materially in his local community. Hospital standardization alone offers him unlimited opportunity to provide better medical care for his patients in the hospital in which he works through continuous progress in applying the principles of the minimum standard. Other activities of the College have also received wide recognition by professional groups and the public as well, and together they present a vast educational program.

The annual meeting of the fellows affords officials of the College an opportunity to report on the work of the organization and to receive suggestions from those who have made possible the conduct of these activities. Every fellow of the College will want to attend this important meeting.

## MEDICAL MOTION PICTURES

Visual education plays an increasingly important rôle in the education of the surgeon. Therefore, an enlarged program of surgical motion pictures will be presented at headquarters which will include the latest available films on a variety of subjects. Schedules will be arranged so as not to conflict with the clinical program at hospitals or the scientific sessions, and will include both sound and silent, standard and color films, all of which have been approved by the Committee on Medical Motion Pictures of the College.

## SPECIAL MEETING OF BOSTON SURGICAL SOCIETY

On the evening of Friday, November 7, in Hancock Hall, which is located midway between the Statler and Copley-Plaza Hotels, the Boston Surgical Society will hold a special meeting to which all fellows of the College and other surgeons attending the Clinical Congress are invited to be present. The occasion of this special meeting of the society is the presentation of the Bigelow Medal to Dr. Allen O. Whipple, of New York, for his outstanding contributions to the advancement of surgery.

## HOSPITAL CONFERENCES

On Monday morning at 10:00 o'clock in the ballroom of the Copley-Plaza Hotel, the first

session of the twenty-fourth annual Hospital Standardization Conference will open the Clinical Congress. The report of the 1941 Hospital Standardization survey—official announcement of the list of approved hospitals and hospitals approved for graduate training in surgery—will be made at this session. Dr. Evarts A. Graham, of St. Louis, president of the College, will preside. In addition there will be interesting discussions on the subjects of "Medical Preparedness," "The Preservation of Our Voluntary System of Hospitals," and "Maintaining the Control and Quality of the Professional Work in the Hospital." On Monday afternoon a panel discussion will deal with the timely subject of "Meeting the Problems of Rendering Adequate Care of the Patient and Maintaining Quality Standards of Service During the Present Period of Preparedness and National Emergency," with Dr. Nathaniel W. Faxon, of Boston, presiding.

The program for succeeding days, fully detailed in the following pages, will hold great interest for members of medical staffs, trustees, administrators, and other hospital personnel. Thus on Tuesday morning four panel discussions will deal with the essentials of efficiency of the hospital in (1) the Obstetrical Department, Dr. John R. Fraser, Montreal, presiding; (2) the Orthopedic Department, Dr. Henry H. Kessler, Newark, New Jersey, presiding; (3) Organization and Functioning of the Medical Staff, Dr. Joseph C. Doane, Philadelphia, presiding, and (4) the Department of Anesthesia, Dr. Ralph T. Knight, Minneapolis, presiding.

On Tuesday afternoon several pertinent subjects will be presented including, "The Organization of a Blood Transfusion Department in a General Hospital" by Drs. Leo M. Zimmerman and Sidney O. Levinson, Chicago. Following these papers a sound motion picture on the subject of "The Proper Use and Care of Hypodermic Needles" will be shown. Tuesday evening's session will be of particular interest to hospital trustees when the subject of the panel discussion will be "The Hospital Trustee in His Relationships and Responsibilities," led by Raymond P. Sloan, of New York.

On Wednesday morning, a joint session with the American Association of Medical Record Librarians will be held, with Dr. Robin C. Buerki, of Philadelphia, presiding. Wednesday evening will be given over to the showing of medical motion pictures for hospital personnel, including the film "White Battalions—Serving All Mankind."

Two important panel discussions will be held on Thursday morning; one on the "Essentials

Pertaining to an Efficient Department of Urology" will be led by Dr. George F. Cahill, New York, and the other "Essentials Pertaining to an Efficient Department of Ophthalmology and Otolaryngology" by Drs. Conrad Behrens and Marvin Jones, of New York. On Thursday afternoon, Drs. Robin C. Buerki, of Philadelphia, will lead a round-table conference on "Pertinent Problems Emanating from a Complete Survey of the Hospital Field." An ample opportunity will be given those present to submit questions which are not on the special program.

In preparing this portion of the program, organizations representing the specialty groups have been invited to participate. Special consideration will be given in this series of meetings to the important subject of graduate training in surgery. It is hoped that through this means the fellows of the College may become better acquainted with its program of hospital activities, which is aimed at improvement of the environment in which the surgeon is working—the hospital.

For Thursday afternoon a series of demonstrations in the local hospitals is being arranged. Those who are acquainted with Boston are fully aware of the inspiration furnished by the privilege of inspecting one of the country's greatest hospital centers. Those who have not had that privilege have a memorable experience in store.

At both the Clinical Congress and the sectional meetings of the College during recent years, the breakfast hospital conferences have been especially well attended. In Boston, such a conference will be held on Tuesday morning when there will be a "Forum on Fundamental Problems of Hospital Administration," sponsored by the American College of Hospital Administrators, in co-operation with the American College of Surgeons.

On Wednesday morning, the breakfast conference will be sponsored by the Boston Medical Record Librarians Association, in co-operation with the College, when there will be held a "Forum on Fundamental Considerations in the Art and Science of Medical Record Keeping." The Thursday morning breakfast conference will be devoted to hospital public relations. The plan is to allow each speaker ten minutes to present his subject, following which everyone will be called upon to give his reaction to the problem under discussion. Attendance at these meetings will necessarily be limited and arrangements will be made for advance registration.

One of the most important features of the hospital conference will be the daily consultation

service from 4:30 to 6:00 p.m. This service affords an opportunity for everyone attending the meeting to consult with recognized leaders in the hospital field on any question or problem on which specific information is desired.

#### PUBLICATION OF PROCEEDINGS

As in former years, the formal papers which are presented at the scientific sessions of the Congress will be presented in a special issue of the official journal of the College, "SURGERY, GYNECOLOGY, AND OBSTETRICS," published in February following the meeting. This issue is furnished without additional charge to all fellows, junior candidates, and others who register for the Congress as invited guests. The papers which are presented in connection with the Hospital Standardization Conference are published in subsequent issues of the *Bulletin* of the American College of Surgeons.

#### ADVANCE REGISTRATION

The hospitals and medical schools of the Boston area afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, attendance at the Congress will be limited to the number that can be comfortably accommodated at the clinics. The limit of attendance will be based on a survey determining the available facilities in the participating hospitals and schools. It is expected, therefore, that surgeons who wish to attend the Congress will register in advance. A registration fee will be required in order to provide funds with which to meet expenses of the meeting. A formal receipt will be issued to each surgeon registering in advance which will be exchanged for a general admission card upon presentation at headquarters during the Congress. This card, which is not transferable, must accompany all requests for clinic tickets and be presented for admission to the scientific sessions.

A resolution adopted by the Board of Regents provides that the registration fee for fellows of the College and endorsed junior candidates shall be \$5.00; that no fee for the 1941 Clinical Congress shall be required of initiates (class of 1941); that the fee for surgeons who are not fellows, attending as invited guests of the College, shall be \$10.00.

As in previous years, admission to clinics and demonstrations in the hospitals and certain of the scientific meetings at headquarters will be controlled by means of tickets. This plan provides for the distribution of visiting surgeons at the various clinics and other meetings, and helps to insure against overcrowding. The number of

clinic tickets issued will be limited in each case to the capacity of the room in which the clinic is held. It should be pointed out that the clinical program as published in the following pages and also in the official program to be distributed at the Congress, obviously cannot include all of the detailed information regarding operative clinics and demonstrations scheduled for the various hospitals. The complete and final program will be provided from day to day, posted in the form of bulletins at headquarters each afternoon for the succeeding day, and published in the *Daily Clinical Bulletin* for distribution each morning. Visiting surgeons are urged to consult the bulletins posted at headquarters and the *Daily Clinical Bulletin* in selecting the clinics they wish to attend, and in making requisitions for clinic tickets. Co-operation in making the clinic ticket plan a success will be greatly appreciated.

#### HEADQUARTERS AND TECHNICAL EXHIBITION

Headquarters for the Congress will be established at the Statler and Copley-Plaza Hotels where there are ample facilities for accommodating the Congress. All of the public rooms have been reserved for the exclusive use of the College during the five-day meeting. Registration for visiting surgeons and their ladies, the Technical Exhibition, executive offices of the College, and certain scientific sessions and medical motion picture exhibitions will be located in the Statler Hotel. Registration for those attending the hospital conference, exhibits of College activities, and the morning, afternoon, and evening hospital conferences will be located in the Copley-Plaza Hotel. The evening scientific sessions on Tuesday, Wednesday, and Thursday will also be held at the Copley-Plaza.

The Technical Exhibition, registration desk for attending surgeons, clinic ticket and information bureau will be located in the ballroom on the mezzanine floor of the Statler Hotel. Additional space for the exhibition will be provided in the Assembly Room and the mezzanine lounge adjacent to the ballroom. Leading manufacturers of surgical instruments and supplies, sutures, dressings, pharmaceuticals, operating room equipment of all kinds, and publishers of medical books will be represented in the exhibition. It will provide an opportunity for surgeons and hospital visitors to carefully inspect the finest modern products of all those industries which are helping to improve the service of hospitals and surgeons.

#### COMMITTEE ON ARRANGEMENTS

Leland S. McKittick	William F. Ladd
Chairman	Frank H. Lahey
Richard H. Sweet	Donald Munro
Secretary	Charles G. Myer
Arthur W. Allen	Frank R. Ober
Edward D. Churchill	Robert B. Osgood
Howard M. Clute	Frank A. Pemberton
E. Granville Crabtree	George L. Tolby, Jr.
W. H. C. Cutler	Frederick H. Verboeff
Frederick C. Irving	Irving J. Walker
	Shields Warren

#### RAILROAD FARES

As no special rates have been authorized by the railroads of the United States or Canada for the 1941 Clinical Congress in Boston, in accordance with the policy adopted by the railroads, no certificates will be required. However, round-trip tickets to Boston, sold at less than double the regular one-way fare, will be available from points in the United States and Canada. Return limit privileges of such round-trip tickets are liberal but are not uniform in all sections of the country. In most instances the return limit is 30 days or more. Surgeons planning to attend the Congress should consult local ticket agents several days in advance of the date of the meeting for complete information as to fares, routes, stopover privileges, etc.

#### BOSTON HOTELS AND THEIR RATES

In addition to the headquarters hotels, the Statler and Copley-Plaza, there are a number of first-class hotels within a short distance of headquarters. These will provide ample facilities at reasonable rates. It is suggested that reservations for hotel accommodations be made well in advance of the meeting. The following hotels are recommended by the committee:

	Minimum Rates with Bath	
	Single	Double
Bellevue, 21 Beacon Street	\$3.00	\$4.50
Bradford, 275 Tremont Street	3.00	4.50
Brunswick, 520 Boylston Street	3.00	4.00
Buckminster, 645 Beacon Street	2.50	4.00
Copley-Plaza, 138 St. James Avenue	4.00	6.00
Copley Square, 47 Huntington Avenue	2.75	4.00
Kenmore, 490 Commonwealth Avenue	3.50	5.00
Lenox, 124 Lexington Street	3.00	3.50
Lincolnshire, 20 Charles Street	3.00	5.00
Parker House, 60 School Street	3.50	5.00
Ritz Carlton, 15 Arlington Street	5.00	8.00
Sheraton, 91 Bay State Road	3.00	5.00
Somerset, 400 Commonwealth Avenue	3.50	6.00
Statler, Park Square	3.50	5.00
Touraine, 62 Boylston Street	3.50	5.00
Vendome, 160 Commonwealth Avenue	3.00	4.00
Westminster, 124 St. James Avenue	2.50	4.00

## HOSPITALS AND REPRESENTATIVES

Beth Israel Hospital—Jacob Fine	Massachusetts Eye and Ear Infirmary—F. H. Verhoef
Beverly Hospital—Richard E. Alt	Massachusetts General Hospital—Arthur W. Allen
Evangeline Booth Maternity Hospital— William J. McDonald	Massachusetts Memorial Hospitals—Frank E. Barton
Boston City Hospital—Otto J. Hermann	New England Baptist Hospital—N. W. Swinton
Boston Lying-in Hospital—Frederick C. Irving	New England Deaconess Hospital—B. P. Colcock
Peter Bent Brigham Hospital—Elliott C. Cutler	New England Hospital for Women and Children— L. D. Adams
Robert Breck Brigham Hospital—John G. Kuhns	New England Medical Center—Samuel H. Proger
Carney Hospital—A. M. Fraser	Newton Hospital—E. D. Leonard
Children's Hospital—Thomas H. Lanman	Palmer Memorial Hospital—L. S. McKittrick
Faulkner Hospital—E. L. Young	Pondville Hospital—E. M. Daland
Free Hospital for Women—Frank A. Pemberton	St. Elizabeth's Hospital—Joseph Stanton
Collis P. Huntington Memorial Hospital—C. C. Simmons	Salem Hospital—Walter G. Phippen
Lakeville State Sanatorium—George W. VanGorder	United States Marine Hospital—R. L. Waugh
Malden Hospital—E. J. Reynolds	United States Naval Hospital—J. J. A. McMullin



## PROGRAMS FOR EVENING SESSIONS

*Presidential Meeting and Convocation—Monday, 8:00 p m —Symphony Hall*

EVARTS A. GRAHAM, M.D., St. Louis; President, American College of Surgeons, Presiding.  
 Processional—Officers, Regents, and Honorary Guests.

Invocation

Address of Welcome. LELAND S. MCKITTRICK, M.D., Boston; Chairman, Committee on Arrangements.

Introduction of Foreign Guests ARTHUR W. ALLEN, M.D., Boston; Vice Chairman, Board of Regents.

Address of Retiring President: American Surgery in a Changing World. EVARTS A. GRAHAM, M.D., St. Louis.

Inauguration of Officers:

President: W. EDWARD GALLIE, M.D., Toronto

First Vice President: CLARENCE G. TOLAND, M.D., Los Angeles.

Second Vice President: ALBERT C. FURSTENBERG, M.D., Ann Arbor.

Presentation of Initiates for Fellowship IRVIN ABELL, M.D., Louisville; Chairman, Board of Regents

Conferring of Fellowships by the President. W. EDWARD GALLIE, M.D., Toronto.

Conferring of Honorary Fellowships. The President.

Medical Records Prize Award.

*Tuesday, 8:00 p m.—Ballroom, Copley-Plaza Hotel*

Annual Oration on Surgery: Some Lessons Learned in the Great War W. EDWARD GALLIE, M.D., Toronto

Use of Female Sex Hormones in Clinical Practice. EDWIN C. HAMBLEY, M.D., Durham, N. C.

The Prevention and Treatment of Tetanus. WARFIELD M. FIROR, M.D., Baltimore

The Care of the Slightly Wounded WILLIAM DARRACH, M.D., New York

*Wednesday, 8:00 p m —Ballroom, Copley-Plaza Hotel*

Subject to be announced GORDON GORDON-TAYLOR, O.B.E., F.R.C.S. (Eng.), London, England

Endocrine Aspects of Chronic Cystic Mastitis. HOWARD C. TAYLOR, JR., M.D., New York

Penetrating Wounds of the Heart and Pericardium. R. ARNOLD GRISWOLD, M.D., and C. H. MAGUIRE, M.D., Louisville

Oration on Fractures and Other Traumas. *The General Surgeon's Approach to Problems Presented by Fractures and Other Traumas.* WALTER ESTELL LEE, M.D., Philadelphia.

*Thursday, 8:00 p m —Ballroom, Copley-Plaza Hotel*

Subject to be announced PROFESSOR PABLO LUIS MIRIZZI, M.D., Cordoba, Argentina.

Carcinoma of the Stomach (*Diagnostic Methods and Therapy*) HOWARD K. GRAY, M.D., Rochester, Minn.

Non-penetrating Wounds of the Abdomen W. L. ESTES, JR., M.D., Bethlehem, Pa.

Adrenal Cortical Tumors; the Types of Non-hormonal and Hormonal Tumors GEORGE F. CAHILL, M.D., New York.

Evaluation of Blood and Blood Substitutes. ALFRED BLALOCK, M.D., Nashville.

## PROGRAMS FOR EVENING SESSIONS

## OPHTHALMOLOGY

*Tuesday, 8:00 p.m.—Copley-Plaza Hotel*

Symposium: Surgery of Heterophoria and Heterotropia.

Preoperative Diagnosis and Treatment. JAMES W. WHITE, M.D., New York.

Recent Advances in the Surgery of Heterotropia. PROFESSOR MOACYR EYCK ALVARO, M.D., Sao Paulo, Brazil.

Surgical Management of Heterophoria. DERRICK T. VAIL, JR., M.D., Cincinnati.

Results of Operation and Causes of Failure. WILLIAM THORNWALL DAVIS, M.D., Washington.

*Thursday, 8:00 p.m.—Copley-Plaza Hotel*

Symposium: Principles of Ophthalmic Surgery.

Surgical Anatomy of the Eye. F. BRUCE FRALICK, M.D., Ann Arbor.

Refinements of General Surgical Technique as Applied to Ophthalmology. CONRAD BERENS, M.D., New York.

Management of Surgical Complications. THOMAS D. ALLEN, M.D., Chicago.

## OPHTHALMOLOGY AND OTORHINOLARYNGOLOGY

*Wednesday, 8:00 p.m.—Copley-Plaza Hotel*

Symposium: Neurological Surgery as Related to the Eye and Ear.

Intracranial Infections and Their Spread from the Ear and from the Sinuses. ALBERT C. FURSTENBERG, M.D., Ann Arbor, Mich.

Retrobulbar Neuritis in Relation to Sinus Disease. JAMES B. COSTEN, M.D., St. Louis.

Tumors of the Acoustic Nerve. BYRON STOOKEY, M.D., New York.

Major Surgery of the Orbit. HOWARD C. NAFFZIGER, M.D., San Francisco.

Interpretation of Perimetric Fields of Vision as Manifested in Intracranial Disease. WALTER I. LILLIE, M.D., Philadelphia.

## OTORHINOLARYNGOLOGY

*Tuesday, 8:00 p.m.—Copley-Plaza Hotel*

Mastoid Diseases in the Light of Chemotherapy. JAMES H. MAXWELL, M.D., Ann Arbor, Mich.

Refinements in the Technique of Laryngectomy. WAITMAN F. ZINN, M.D., Baltimore.

The Otology of Craniocerebral Injuries. WILLIAM E. GROVE, M.D., Milwaukee, Wis.

*Thursday, 8:00 p.m.—Copley-Plaza Hotel*

Symposium: The Salivary Gland.

Benign Tumors. ALBERT O. SINGLETON, M.D., Galveston, Texas

Malignant Tumors. LEROY A. SCHALL, M.D., Boston.

Infections. AUGUST L. BECK, M.D., New Rochelle, N. Y.

## PROGRAMS FOR AFTERNOON SESSIONS

### SYMPOSIUM ON FRACTURES AND OTHER TRAUMAS

*Wednesday, 2:00 p.m.—Copley-Plaza Hotel*

- ROBERT H. KENNEDY, M.D., New York; Chairman, Committee on Fractures and Other Traumas, Presiding  
 Gunshot Wounds of the Abdomen. AMBROSE H. STORCK, M.D., New Orleans.  
 A Critical Survey of Ten Years' Experience with Fractures of the Neck of the Femur. MATHER CLEVELAND, M.D., New York  
 Factors in the Choice of Material for Bone Plates and Screws CHARLES S. VENABLE, M.D., San Antonio, Texas.  
 Treatment of Burns GROVER C. FENBERTH, M.D., Detroit.  
 Results in Cases of Compound Fractures Followed by Osteomyelitis. STANTON K. LIVINGSTON, M.D., Veterans Administration Facility, White River Junction, Vermont

## GROUP CLINICAL CONFERENCES

### OPHTHALMOLOGY AND OTORHINOLARYNGOLOGY

*Tuesday, 11:00 a.m.*

- Surgery of Squint JOHN H. DUNNINGTON, M.D., New York, Presiding.  
 Treatment of Sinus Disease in Children. SAMUEL SALINGER, M.D., Chicago, Presiding

*Wednesday, 11:00 a.m.*

- Surgery of the Tear Passages WALTER S. ATKINSON, M.D., Watertown, N.Y., Presiding  
 Indications for Surgery of the Nose and Throat in Diabetics WESTLEY M. HUNT, M.D., New York, Presiding

*Thursday, 11:00 a.m.*

- Surgery of the Orbit ALGERNON B. REESE, M.D., New York, Presiding  
 Surgical Treatment of Deafness SAMUEL J. KOPETZKY, M.D., New York, Presiding

## PANEL DISCUSSIONS

- Injuries to the Spine ERIC OLDBERG, M.D., Chicago, Presiding  
 Collaborators: FREDERICK A. JOSTES, M.D., St. Louis, HOWARD C. NAFFZIGER, M.D., San Francisco, J. E. M. THOMSON, M.D., Lincoln, Neb.  
 Diseases of the Esophagus ALTON OCHSNER, M.D., New Orleans, Presiding  
 Collaborators: CARL EGGERS, M.D., New York, FRANK H. LAHEY, M.D., Boston, GABRIEL TUCKER, M.D., Philadelphia  
 Thyroid Disease Associated with Congestive Failure WILLIAM B. PARSONS, M.D., New York, Presiding  
 Collaborators: RICHARD B. CATTELL, M.D., Boston, ROBERT S. DINSMORE, M.D., Cleveland, MERRILL N. FOOTE, M.D., Brooklyn.  
 Postoperative Pulmonary Complications LEO ELOESSER, M.D., San Francisco, Presiding  
 Collaborator: HENRY K. BECHER, M.D., Boston.  
 Lung Surgery STUART W. HARRINGTON, M.D., Rochester, Minn., Presiding  
 Collaborators: RICHARD H. MEADE, JR., M.D., Philadelphia, HAROLD NEUNOF, M.D., New York; WILLIAM F. RIENHOFF, JR., M.D., Baltimore

Gastric Ulcer. URBAN MAES, M.D., New Orleans, Presiding.

Collaborators: RALPH COLP, M.D., New York; VERNE C. HUNT, M.D., Los Angeles; GEORGE P. MULLER, M.D., Philadelphia.

Experience with the Miller-Abbott Tube. ALLEN O. WHIPPLE, M.D., New York, Presiding.

Collaborators: WILLIAM O. ABBOTT, M.D., Philadelphia; CHARLES G. JOHNSTON, M.D., Detroit; ANGUS McLACHLIN, M.D., Toronto.

Optimum Time for Operation with Special Consideration of Acute Gallbladder Attacks. HENRY F. GRAHAM, M.D., Brooklyn, Presiding.

Collaborators: FRANK GLENN, M.D., New York; CHARLES GORDON HEYD, M.D., New York; E. MACDONALD STANTON, M.D., Schenectady, N. Y.

Penetrating Abdominal Wounds Caused by Trauma. ARTHUR M. SHIPLEY, M.D., Baltimore, Presiding.

Collaborators: E. CLARENCE MOORE, M.D., Los Angeles; ELKIN L. RIPPY, M.D., Nashville; ALBERT O. SINGLETON, M.D., Galveston.

Disruption of Abdominal Wounds. FRANK GLENN, M.D., New York, Presiding.

Collaborators: LAWRENCE S. FALLIS, M.D., Detroit; L. KRAEER FERGUSON, M.D., Philadelphia; HILGER P. JENKINS, M.D., Chicago.

The Sulfonamide Group in Abdominal Surgery. FREDERICK A. COLLIER, M.D., Ann Arbor, Presiding.

Collaborators: PERRIN H. LONG, M.D., Baltimore; I. S. RAVDIN, M.D., Philadelphia; JAMES E. THOMPSON, JR., M.D., New York.

Intestinal Obstruction in Children. WILLIAM E. LADD, M.D., Boston, Presiding.

Collaborators: WILLIS D. GATCH, M.D., Indianapolis; GEORGE B. PACKARD, M.D., Denver; GROVER C. PENBERTHY, M.D., Detroit.

The Management of the Perforated Appendix, Early and Late. HENRY K. RANSOM, M.D., Ann Arbor, Mich., Presiding.

Collaborators: J. MONTGOMERY DEEVER, M.D., Philadelphia; CLARENCE E. GARDNER, M.D., Durham, N. C.; E. ERIC LARSON, M.D., Los Angeles.

Surgical Diseases of the Colon. CHARLES W. MAYO, M.D., Rochester, Minn., Presiding.

Collaborators: THOMAS G. ORR, M.D., Kansas City, Mo.; HOWARD PATTERSON, M.D., New York; J. WILLIAM THOMPSON, M.D., St. Louis.

Management of Abortion. CONRAD G. COLLINS, M.D., New Orleans, Presiding.

Collaborators: RALPH E. CAMPBELL, M.D., Madison, Wis.; JOHN R. FRASER, M.D., Montreal; H. CLOSE HESSELTINE, M.D., Chicago.

Treatment of Chronic Cervicitis. GEORGE H. GARDNER, M.D., Chicago, Presiding.

Collaborators: JOHN C. BURCH, M.D., Nashville; J. MASON HUNDLEY, JR., M.D., Baltimore; JOE V. MEIGS, M.D., Boston.

Management of Calcium Urolithiasis. NORMAN W. ROOME, M.D., London, Ont., Presiding.

Collaborators: HENRY O. MERTZ, M.D., Indianapolis; JOHN K. ORMOND, M.D., Detroit; A. J. SCHOLL, M.D., Los Angeles.

Traumas to the Head. FRANCIS C. GRANT, M.D., Philadelphia, Presiding.

Collaborators: CHARLES BAGLEY, JR., M.D., Baltimore; COBB PILCHER, M.D., Nashville; JAMES C. WHITE, M.D., Boston.

Fractures of the Facial Bones. LLOYD NOLAND, M.D., Fairfield, Ala., Presiding.

Collaborators: ROBERT H. IVY, M.D., Philadelphia; CARL W. WALDRON, M.D., Minneapolis; Charles, H. WILSON, M.D., New Orleans.

- Treatment of Acute Suppurative Tenosynovitis of the Fingers, Palm, and Forearm. HUGH AUCHINCLOSS, M D, New York, Presiding  
Collaborators: WILLIAM E. BROWNE, M D, Boston; J. H. COUCH, M D, Toronto; JAMES M. WINFIELD, M D, Detroit.
- The Treatment of the Wound in Compound Fractures CLAY RAY MURRAY, M D., New York, Presiding  
Collaborators: R. ARNOLD GRISWOLD, M D., Louisville, J. ALBERT KEY, M.D., St. Louis, HENRY C MARBLE, M D., Boston
- Principles Involved in Hip Joint Arthroplasty. M. N. SMITH PETERSEN, M D, Boston, Presiding  
Collaborators: CARL E. BADGLEY, M D, Ann Arbor, Mich.; GEORGE E. BENNETT, M D, Baltimore, PHILIP D. WILSON, M D, New York.
- Developments in the Field of Poliomyelitis Research. EDWARD L. COMPERE, M D., Chicago, Presiding  
Collaborators: FRFMONT A. CHANDLER, M.D., Chicago; CHARLES L. LOWMAN, M.D., Los Angeles, OSCAR L. MILLER, M D., Charlotte, N C
- Advances in Skin Grafting EARL C. PADGETT, M D., Kansas City, Mo., Presiding  
Collaborators JAMES BARRETT BROWN, M D, St. Louis MICHAEL L. MASON, M D, Chicago, HANS MAY, M D., Philadelphia
- Treatment of Contaminated and Infected Wounds FRASER B. GURD, M D, Montreal, Presiding  
Collaborators JOSEPH E. HAMILTON, M D, Louisville, MICHAEL L. MASON, M D, Chicago FRED ERICK S. WETHPRELL, M D, Syracuse, N Y
- Chemotherapy in Wound Healing EDWARD L. HOWES, M D, New York, Presiding  
Collaborators HILGER P. JENKINS, M D, Chicago, FRANK L. MELENEY, M D, New York; J. ROSS VEAL, M D, Washington
- Continuous Spinal Anesthesia WILLIAM T. LEMMON, M D, Philadelphia, Presiding  
Collaborators: H. H. BRADSHAW, M D, Winston Salem, N C, RALPH T. KNIGHT, M D., Minneapolis; EDWARD B. TUOHY, M D, Rochester, Minn
- Anesthesia in War KENNETH C. MCCARTHY, M D, Toledo, Presiding
- Anesthesia for Surgical Procedures within the Upper Abdomen RALPH M. TOVELL, M D, Hartford, Conn., Presiding  
Collaborators HENRY K. BEECHER, M D, Boston, HOWARD K. GRAY, M D, Rochester, Minn., HENRY S. RUTH, M D, Merion, Pa
- Transfusion and Blood Substitutes, Especially Plasma, in the Prevention and Treatment of Shock ROY D. MCCLURE, M D, Detroit, Presiding  
Collaborators NORMAN E. FREEMAN, M D, Philadelphia JOHN SCLODDER, M D, New York, OWEN H. WANGENSTEEV, M D., Minneapolis
- Contributions to Medical Progress through Postmortem Examinations ALAN R. MORITZ, M D, Boston, Presiding  
Collaborators A. D. GETTLER, New York, HARRISON S. MARILAND, M D, Newark, N J
- Vitamins in Surgery WARREN H. COLE, M D, Chicago, Presiding  
Collaborators EMILE HOLMAN, M D, San Francisco, WALTER ESTELL LEE, M D, Philadelphia, CHARLES C. LUND, M D, Boston
- Graduate Training in Surgery in Hospitals ROBIN C. BUERKI, M D, Philadelphia, Presiding  
Collaborators DAVID H. BALLON, M D, Montreal, GEORGE F. CAHILL, M D, New York, EDWARD D. CHURCHILL, M D, Boston, JOHN R. FRASER, M D, Montreal, W. EDWARD GALLIE, M D., Toronto, HARRY S. GRADLE, M D, Chicago, DALLAS B. PEMISTEE, M D, Chicago, STANLEY J. SEEGER, M D, Milwaukee, Wis., PHILIP D. WILSON, M D., New York

## ANNUAL HOSPITAL STANDARDIZATION CONFERENCE

*Monday, 10:00 a.m.—Copley-Plaza Hotel*

EVARTS A. GRAHAM, M.D., St. Louis; President, American College of Surgeons, presiding.

Address of the President—The Hospital Program of the American College of Surgeons.

Report of the 1941 Hospital Standardization Survey—Official Announcement of the List of Approved Hospitals. IRVIN ABELL, M.D., Louisville; Chairman, Board of Regents, and EARLE W. WILLIAMSON, M.D., Chicago; Assistant Director, American College of Surgeons.

Report on Graduate Training in Surgery. DALLAS B. PHEMISTER, M.D., Chicago; Chairman, Committee on Graduate Training in Surgery, and HAROLD EARNHEART, M.D., Chicago; Assistant Director, American College of Surgeons.

Important Legislative, Preparedness and Emergency Problems Now Facing Hospitals. BERT W. CALDWELL, M.D., Chicago; Executive Secretary, American Hospital Association.

The Preservation of Our Voluntary System of Hospitals. REV. ALPHONSE W. SCHWITALLA, S. J., St. Louis; President, Catholic Hospital Association.

National Events—Their Effect on Personnel Relations. FRANK J. WALTER, Denver.

The Responsibility of the Medical Staff in Maintaining Control and Quality of the Professional Work in the Hospital. MERRILL N. FOOTE, M.D., Brooklyn.

The Preparedness Program for Hospitals. JAMES A. HAMILTON, New Haven, Conn.

*Monday, 2:00 p.m.—Copley-Plaza Hotel*

Panel Round Table Conference: Meeting the Problems of Rendering Adequate Care of the Patient and Maintaining Quality Standards of Service During the Present Period of Preparedness and National Emergency. NATHANIEL W. FAXON, M.D., Boston, presiding.

Discussion from the viewpoint of personnel: Medical Staff. NORBERT A. WILHELM, M.D., Boston. Resident Medical Staff. CLAUDE W. MUNGER, M.D., New York.

Nursing Staff. SALLY JOHNSON, R.N., Boston.

Discussion from the standpoint of medical, surgical and hospital equipment, instruments and supplies:

Scientific Equipment and Instruments. D. H. PALMER, New York.

Surgical Dressings, Rubber Goods and Other Supplies. L. M. ARROWSMITH, Brooklyn.

Surgical Ligatures, Pharmaceuticals and Chemicals. EVERETT W. JONES, Albany, N. Y.

Discussion from the standpoint of operating costs:

Foodstuffs, Supplies of All Kinds, Commodities, etc. MIRIAM CURTIS, R.N., Syracuse, N. Y.

Salaries and Wages. ABRAHAM OSEROFF, Pittsburgh.

Supplementary Revenue: Subsidies, Gifts, Donations, Endowments, etc. OLIVER H. BARTINE, Bridgeport, Conn.

General Discussion. Other related subjects may be presented.

*Monday, 4:30 p.m.—Copley-Plaza Hotel*

Consultation Service. Opportunity will be afforded everyone attending the Hospital Standardization Conference to consult with recognized leaders in the hospital field, on any question or problem on which specific information is desired. A consultation service will be available at the time and place specified in the program, by means of pre-arranged information stations, on six different phases of hospital service daily. This service will be provided by leaders in the various fields of hospital administration and management.

Administrative Practices and Policies. EDGAR C. HAYHOW, Paterson, N. J.

Anesthesia Service. E. B. TUOHY, M.D., Rochester, Minn.

Clinical Laboratory and Pathological Service. WILMAR M. ALLEN, M.D., Hartford, Conn.

Control of Major Surgery in the Hospital. E. MACDONALD STANTON, M.D., Schenectady, N. Y.

Food Service in the Hospital—Diet Therapy. GENEVA MARBLE, Boston.

Hospital Preparedness in the Defense Program. OLIVER G. PRATT, Salem, Mass.

*Tuesday, 7:15 a.m.—Copley-Plaza Hotel*

Breakfast Conference, Sponsored by the American College of Hospital Administrators in co-operation with the American College of Surgeons: Forum on Fundamental Problems of Hospital Administration. SCOTT WHITCHER, New Bedford, Mass., presiding.

Discussion from the following aspects:

Relation of Personal Qualities and Attitudes to Successful Hospital Administration. G. HARVEY AGNEW, M.D., Toronto, Ont.

Critical Analysis of Present Methods of Training for Hospital Administration. E. M. BLUESTONE, M.D., New York.

General Discussion. Opened by GERHARD HARTMAN, Chicago.

*Tuesday, 9:30 a.m.—Copley-Plaza Hotel*

Panel Discussion: Essentials Pertaining to an Efficient Obstetrical Department in the Hospital. JOHN R. FRASER, M.D., Montreal, leader. Collaborators: JOSEPH L. BAER, M.D., Chicago; CLARA M. KONRAD, R.N., Jersey City; JAMES R. MILLER, M.D., Hartford.

Topics for discussion: Accommodations, facilities and equipment of a modern obstetrical department. Supervision and management of the obstetrical department. Personnel—resident, medical and nursing staffs. Qualifications of the medical staff in the practice of obstetrics within the hospital. Control of the clinical work. Essentials of a complete obstetrical record. Control of infections and complications. Periodic analytical summaries of end results. Care of the newborn. Graduate training in obstetrics.

Panel Discussion: Essentials Pertaining to an Efficient Department of Orthopedic Surgery in the Hospital. HENRY H. KESSLER, M.D., Newark, N. J., leader. Collaborators: FRANK D. DICKSON, M.D., Kansas City, Mo.; FREMONT A. CHANDLER, M.D., Chicago.

Topics for discussion: Accommodations, facilities and equipment of a department of orthopedic surgery in a hospital. Supervision and management of the department of orthopedic surgery. Personnel—resident, medical and nursing staffs. Qualifications of the medical staff to do orthopedic surgery. Control of the clinical work of the department of orthopedic surgery. Essential contents of the medical record in orthopedic surgery. Review and analysis of the clinical work of the department of orthopedic surgery. Splint and brace shop. Follow up and study of end results. Graduate training in orthopedic surgery.

*Tuesday, 11 00 a m—Copley-Plaza Hotel*

Panel Discussion Organization and Functioning of the Medical Staff. JOSEPH C. DOANE, M.D., Philadelphia, leader. Collaborators: STANLEY J. SEGER, M.D., Milwaukee; JULIUS H. COMFOR, York, Pa.; CHARLES B. PUESTOW, M.D., Chicago; ALLAN CRAIG, M.D., Bangor, Maine.

Topics for discussion: Standards of qualifications in making appointments to the medical staff. Procedure in making appointments to the medical staff. Legal responsibility of the hospital in respect to the professional work of the hospital. Supervision and control of major surgery and major obstetrics. Basic considerations in making promotions on the medical staff of the hospital. Essential features in conducting the medical staff conference. Maintaining adequate medical records. Increasing the number of consultations in hospital practice. Supervision of the work of the resident medical staff. Responsibility of the senior members of the medical staff in instructing junior members.

Panel Discussion Essentials Pertaining to an Efficient Department of Anesthesia in the Hospital. RALPH T. KNIGHT, M.D., Minneapolis, leader. Collaborators: RALPH M. TOVELL, M.D., Hartford; HENRY RUTH, M.D., Merion, Pa.; HENRY M. POLLOCK, M.D., Boston.

Topics for discussion: Accommodations, facilities and equipment of the department of anesthesia in the hospital. Supervision and management of the department of anesthesia. Essential qualifications for the efficient administration of anesthesia. Anesthesia records to be maintained. A critical analysis of newer types of anesthetics and methods of administration. Hazards associated with the administration of anesthetics. Training of interns and residents in the administration of anesthetics. Follow-up and study of end results in the administration of anesthetics. Handling of emergency anesthetics. Graduate training in anesthesiology.

*Tuesday, 2 00 p m—Copley-Plaza Hotel*

ALBERT G. ENGELBACH, M.D., Cambridge, Mass., presiding.

The Organization of a Blood Transfusion Department in a General Hospital. LEO M. ZIMMERMAN, M.D., and SIDNEY O. LEVINSON, M.D., Chicago.

Organization and Use of the Medical Library by the Medical Staff and Personnel of the Hospital. L. MARGUFRITTE PRIME, Chicago.

A Successful Plan in Handling the Personnel Health Service in the Hospital. JOSEPH G. NORBY, Milwaukee.

The Control and Assignment of Duties of Non-Professional Workers in the Hospital. FRANCES C. LADD, R.N., Boston.

*Tuesday, 4 30 p m—Copley-Plaza Hotel*

Consultation Service:

Internships and Residencies. M. G. WESTMORELAND, M.D., Chicago.

Medical Records. EDNA K. HOFFMAN, R.R.L., Chicago.

Medical Social Service. MABEL WILSON, Boston.

Medical Staff Problems. PAUL S. FERGUSON, M.D., Chicago.

Sterilization of Surgical Dressings, Instruments, Rubber Goods, Supplies, etc. SAMUEL R. D. HEWITT, M.D., St. John, New Brunswick.

*Tuesday, 8 00 p m—Copley-Plaza Hotel*

Panel Discussion The Hospital Trustee in his Relations and Responsibilities. RAYMOND P. STON, New York, leader. Collaborators: FRANK O. ROBSON, Southbridge, Mass.; JOHN MACGREGOR, Boston; SAMUEL STEWART, Lewiston, Maine; CHARLES F. WILKINSKY, M.D., Boston.

Topics for discussion: Qualifications of the ideal hospital trustee. Acquiring essential knowledge concerning hospital administration. Relationship of the hospital trustee to (a) the administration, (b) the medical staff. The problem of the hospital trustee in selecting a hospital administrator. The trustee's responsibility in the increasing financial responsibility of the hospital. The hospital trustee's approach to problems with possible legal or liability significance. Meeting the responsibility of the present demands on hospitals incident to the preparedness program. Preparation and conduct of the monthly meeting of the board of trustees. Monthly and annual reports. The trustee's participation in public relations of the hospital.

Motion picture preview White Battalions—Serving All Mankind.

*Wednesday, 7 45 a m—Copley-Plaza Hotel*

Breakfast Conference, Sponsored by the Boston Medical Record Librarians Association in co-operation with the American College of Surgeons. Forum on Fundamental Considerations in the Art and Science of Medical Record Keeping. W. FRANKLIN WOOD, M.D., Waverley, Mass., presiding.

Discussion from the following aspects:

A Critical Analysis of the Present Ways and Means of Training Medical Record Librarians. SISTER M. LORETTA, R.R.L., Duluth, Minn.

The Place of the Medical Record Librarian in the Hospital Organization. MARGARET DeBois, M.D., Chicago.

What the Medical Record Librarian Can Contribute towards Making a Success of Her Career. MARGARET TAYLOR, R.R.L., Rochester, N.Y.

*Wednesday, 9 30 a m—Copley-Plaza Hotel*

Joint Conference with American Association of Medical Record Librarians. ROBIN C. BUERKI, M.D., Philadelphia, presiding.

Our Challenge—Good Medical Records in Our Hospitals. ANNA C. SCHULZE, R.R.L., Philadelphia.

The Role of the Record Librarian in the Changing World. SISTER MARY SEVATIA, R.R.L., St. Louis.

The Preparation of Medical Statistics and Special Studies for the Medical Staff. MARY M. NEWTON, R.R.L., Evanston, Ill.

An Analysis of the Present Problems of Securing Adequate Medical Records in Hospitals, and Their Practical Solution. PAUL B. FERGUSON, M.D., Chicago.





# PRELIMINARY CLINICAL PROGRAM

## GENERAL SURGERY

### Monday

#### BOSTON CITY HOSPITAL

- Staff—2 Symposium: Vascular disease  
 S J G NOWAK—2 Experimental hypertension.  
 E A. EDWARDS—2 30 Thrombophlebitis in unusual forms  
 E E. O'NEIL—3 Lumbar sympathectomy for vascular disease.  
 D C GOLDFARB—3 30 False aneurysm of femoral artery  
 T. LEARY—4 Pathological aspects of vascular disease  
 F. E. O'NEIL—4 30 Refrigeration in gangrene of lower extremities

#### COLLIS P. HUNTINGTON MEMORIAL HOSPITAL

- Staff—2 15 Dry clinic  
 JOSEPH C. AUB Recent advances in our knowledge of bone diseases  
 CHANNING C. SIMMONS Malignant tumors of bone  
 RICHARD DRESSER Radiographic demonstration of bone tumors and certain rare forms of skeletal disease  
 CHARLES E. DUNLAP Carcinogenic agents  
 CLIFFORD C. FRANSEEN Industrial cancer

#### MASSACHUSETTS GENERAL HOSPITAL

- H K BEECHER and associates—2 Dry clinic Anesthesia and related subjects  
 H. K. BEECHER—2 Use of ether in the presence of pulmonary tuberculosis, anesthesia for transpleural gastric surgery  
 JULIA G. ARBWOOD—2 25 Fractional spinal anesthesia  
 H K BEECHER—2 35 Anesthesia and shock  
 Staff—3 10 Discussion  
 EDWARD B. BENEDICT—3 30 Endoscopy, bronchoscopy and esophagoscopy with special emphasis on the two newer endoscopic methods, gastroscopy and peritoneoscopy, demonstration with lantern slides and patients  
 Staff—2 Symposium Peripheral vascular disease, varicose veins and their complications  
 H H FAXON—2 Fundamental considerations, anatomy, physiology, etiology, examination  
 R. H. THOMPSON—2 15 Late results following treatment of uncomplicated varicose veins  
 H H FAXON—2 30 Present concept of treatment  
 R R LINTON—2 45 Chronic and recurrent ulceration of lower extremities, etiological factors and classification, present concept of treatment  
 Staff—3 30 Discussion  
 H H FAXON, R H THOMPSON, and R R LINTON—4 Operations: Peripheral vascular  
 F. M. DALAND, A O HAMPTON, and associates—2 Dry clinic Tumors  
 A O HAMPTON—2 Roentgen diagnosis of cancer of the lung  
 G W HOLMES—2 15 Roentgen treatment of cancer of the lung  
 J V MEIGS—2 30 Changing concepts in the treatment of cancer of the cervix  
 E. M. DALAND—2 45 The locus of recurrence in cancer of the breast

- R. SCHATZKE—3 End results of roentgen therapy in cancer of the larynx  
 L L ROBBINS—3 15 The treatment of polycythemia vera by spray radiation  
 T B MALLORY—3 30 Malignant ulcers of the stomach  
 C E. WELCH—3 45 Gastric ulcers in relation to gastric cancer  
 J R. LINGLEY—4 Comparison of skin effect on the albino rat of 200 k v. and 1200 k v. roentgen ray.  
 G W TAYLOR—4 15 The value of regional dissection in cancer cases

#### NEW ENGLAND BAPTIST HOSPITAL

- H D ADAMS and N W SWINTON—1 30 Operative clinic  
 Thyroid, stomach, colon, rectum and biliary tract.  
 U H EVERSOLE, LEO V HAND, and M J NICHOLSON—1 30 Demonstrations: Anesthesia

#### NEW ENGLAND DEACONESS HOSPITAL

- H D ADAMS and N W SWINTON—1 30 Operative clinic  
 Thyroid, stomach, colon, rectum, and biliary tract  
 U H EVERSOLE, LEO V HAND, and M J NICHOLSON—1 30 Dry clinic Anesthesia in thyroid surgery, including intratracheal anesthesia, pre-operative and post-operative medication, recent developments in spinal anesthesia  
 CARL SOUDERS Postoperative pulmonary complications  
 JAMES EVANS Thrombophlebitis and pulmonary embolism

#### NEW ENGLAND MEDICAL CENTER

- (Joseph H Pratt Diagnostic Hospital)  
 Staff—2 Dry clinic  
 JOSEPH H PRATT—2 Value of secretin test in diagnosis of pancreatic disease  
 WILLIAM DAMESIEK—2 30 Indications for splenectomy, case reports  
 JOHN D. ADAMS—3 Various conditions found in the hip joint following injury  
 EDWARD L. YOUNG—3 30 Peritoneoscopy

#### PALMER MEMORIAL HOSPITAL

- Staff—2 Symposium: Carcinoma of the breast  
 CLIFFORD C. FRANSEEN End results of surgical treatment  
 L S MCKITTRICK Interstitial irradiation treatment of carcinoma of the breast with platinum radium needles  
 J H MARKS X-ray therapy of carcinoma of the breast  
 SHIELDS WARREN Relation between chronic cystic mastitis and carcinoma of the breast

### Tuesday

#### BETH ISRAEL HOSPITAL

- Staff—9 Dry clinic  
 ARNOLD STARR Biliary tract disease, left sided pain  
 C G MIXTER Technique of immediate cholangiography, motion pictures  
 L A HERMANSON Cholangiography, indications for and end results  
 H A FRANK Advantages of intravenous synthetic vitamin K<sub>1</sub> over other vitamin K preparations  
 A M SELIGMAN Vitamin P in capillary fragility

# PRELIMINARY PROGRAM FOR 1941 CLINICAL CONGRESS

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Staff—10:30. Operative clinic:

- C. G. MIXTER. Cholecystectomy and cholangiography.
- JACOB FINE. Cholecystectomy, transverse incision.
- L. H. NASON. Peritoneoscopy, spinal anesthesia.
- ARNOLD STARR. Peritoneoscopy, local anesthesia.

Staff—2. Dry clinic:

- MAX DAVIS. Ovarian tumors with endocrine effects.
- R. B. DAVIDOFF. Relationship of cystic disease of the breast to disease of the uterus and adnexa.
- L. A. HERMANSON. Comparative merits of the vaginal smear and endometrial biopsy in diagnosis of ovarian function.
- S. L. CARGILL. Hyperparathyroidism.
- D. D. BERLIN. Carcinoma of the thyroid.
- M. F. LESSES. Complications of thyroid surgery.
- S. L. CARGILL. Management of recurrent and persistent thyrotoxicosis.
- D. D. BERLIN. The avoidance of complications in thyroid surgery.

SCIENTIFIC EXHIBIT (Daily, 9 to 5)

- JOSEPH GOODMAN. Pathogenic fungi in foot infections.
- H. F. FRIEDMAN. Malignant disease before and after treatment by radiation.
- ABRAHAM RUDY and S. R. MUELLNER. Neurogenic bladder in diabetes mellitus.
- JULIUS LOMAX. Action of autonomic drugs on the gastrointestinal and genito-urinary tracts.
- S. A. ROBINS. Urethrography and cystography.
- W. S. ALTMAN and L. A. HERMANSON. Cholangiography.
- LEONARD NATHAN and KURT THOMA. Cysts and tumors of mouth and jaw.
- JULIUS LOMAX. Cerebral arteriography.
- A. STARR and H. FRANK. Venography in deep phlebitis of lower leg.
- S. HANFLIG. Mechanical device for reduction of Colles' fracture.

## BOSTON CITY HOSPITAL

- Staff—2. Dry clinic: Gastric lesions.
- W. R. MORRISON—2. Gastrojejuno-colonic fistula.
- C. W. McCLURE—2:30. Gastroscopy, kodachrome pictures.
- A. R. KIMPTON—3. Cancer of stomach.
- W. R. MORRISON—3:30. Perforated peptic ulcer.
- E. E. O'NEIL—4. Transpleural approach for carcinoma of upper end of stomach.
- T. W. WICKHAM—4:30. Cholecystitis and its relation to peptic ulcer. Review of 600 cholecystectomies.

## PETER BENT BRIGHAM HOSPITAL

- ELLIOTT C. CUTLER and ROBERT E. GROSS—9. Operations: Ligation of patent ductus arteriosus; pericardiectomy.
- ELLIOTT C. CUTLER and associates—10. Symposium: Surgery of the heart and blood vessels.
- C. SIDNEY BURWELL. Forms of heart disease amenable to surgery.
- SAMUEL A. LEVINE. Cardiac disease simulating surgical conditions of the abdomen and vice versa.
- EUGENE C. EPPINGER. Indications for surgery for patent ductus arteriosus.
- ROBERT E. GROSS. Surgical treatment of patent ductus arteriosus.
- ELLIOTT C. CUTLER. The technique of pericardiectomy.
- MERRILL C. SOSMAN. The rôle of the roentgenologist in cardiac surgery.
- JOHN HOMANS. Peripheral vascular disease.
- MARSHALL N. FULTON. Angioma of skeletal muscle.
- DAVID CHEEVER—2. Surgical anatomy of the abdomen.

## CHILDREN'S HOSPITAL

- WILLIAM E. LADD and associates—10:30. Dry clinic: Diseases of the gastro-intestinal tract in childhood, followed by questions and discussion.
- WILLIAM E. LADD. Atresia, stenosis, and malrotation.
- THOMAS H. LANMAN. Pyloric stenosis.
- ROBERT E. GROSS. Intussusception.
- HENRY W. HUDSON, JR. Appendicitis.

## MASSACHUSETTS GENERAL HOSPITAL

- A. W. ALLEN and associates—8. Symposium: Gastric lesions.
- C. M. JONES—8. Medical considerations.
- A. O. HAMPTON and associates—8:30. Roentgenological studies.
- E. B. BENEDICT—8:50. Gastroscopy and peritoneoscopy.
- C. E. WELCH—9:10. Gastric ulcer.
- LANGDON PARSONS—9:30. Cancer of the stomach.
- R. H. SWEET—9:50. Transthoracic gastrectomy.
- A. W. ALLEN—10:10. Surgical procedures for gastric lesions.
- Staff—10:30. Operations: Gastric resections for benign and malignant lesions.
- H. H. FAXON, HORATIO ROGERS, and associates—9. Symposium: Acute appendicitis.
- HORATIO ROGERS. Present status; chief factors in present mortality rates, late diagnosis and/or treatment, of faulty appraisal of individual patients, rigid policies of treatment, faulty technique, type of incision.
- W. D. SMITH. Appendicitis in general medical practice.
- HORATIO ROGERS. Appendiceal peritonitis before localization.
- H. H. FAXON. Appendiceal peritonitis after localization.
- CHAMP LYONS. The rôle of bacteriology and chemotherapy in appendicitis.
- R. R. LINTON. Special aspects of appendicitis in young children.

Staff—11. Operative clinic.

- L. S. McKITTRICK and associates—2. Symposium: Surgery of the colon and rectum.
- L. S. McKITTRICK—2. Operations for carcinoma of the rectum and their indications.
- A. W. ALLEN—2:20. The management of carcinoma of the colon.
- E. P. HAYDEN—2:40. The complications of diverticulitis of the sigmoid and their management.
- ROY E. MABREY—3. The operative and non-operative management of internal hemorrhoids.
- Staff—3:20. Discussion.
- Staff—3:40. Operative clinic.
- CHAMP LYONS and FRANK L. MELENEY (New York)—2. Dry clinic: Surgical infections.

## MASSACHUSETTS MEMORIAL HOSPITALS

- HOWARD M. CLUTE, CLIFFORD D. HARVEY, CHARLES SZIKLAS, FRANK E. BARTON, and HOLLIS L. ALBRIGHT—8. Operative clinic: Thyroid, gall-bladder, stomach, and colon.
- ELEANOR FERGUSON, REGINALD HUNT, and M. JEAN BLACK. Demonstrations: Anesthesia.
- Staff—10. Symposium: Management of blood-bank.
- FRANK E. BARTON. Management of a blood-bank in a small hospital.
- CHARLES BRANCH. Correlation of the hospital laboratory with the blood-bank.
- JOHN SCUDDER (New York). Studies in treatment of shock with plasma and serum.
- CORNELIUS P. RHODES (New York). Present application and future development of blood substitute therapy.

- PHILLIPS L. BOND—10. Dry clinic. Lymphogranuloma venereum with rectal involvement
- FRANK L. BARTON—2. Demonstration of transfusion service
- Staff—2. Symposium. Surgery of the biliary tract
- KNOWLES LAWRENCE—1. Intravascular disease of the liver simulating cholecystitis
- HOLLIS L. ALDRICH—1.30. Non calculous gall bladder
- THOMAS J. ANGLEW—2.40. Complications of common duct surgery.
- FRANK LEITCHNER—3. Duodenal drainage in diagnosis of biliary tract disease
- CHESTER KETTER—3.30. Liver abscess as a cause of prolonged fever.
- HOWARD M. CLUTE—3.40. Stricture of the bile ducts

#### NEW ENGLAND BAPTIST HOSPITAL

- F. H. LANEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCROCK—0. Operative clinic. Thyroid, stomach, colon, and biliary tract
- U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—0. Anesthesia demonstrations. Regional, spinal, continuous spinal, and general
- H. D. ADAMS and N. W. SWINTON—1.30. Operative clinic. Thyroid, stomach, colon, rectum, and biliary tract
- U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1.30. Demonstrations. Anesthesia

#### NEW ENGLAND DEACONESS HOSPITAL

- F. H. LANEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCROCK—0. Operative clinic. Thyroid, stomach, colon, and biliary tract
- U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—0. Anesthesia demonstrations. Regional, spinal, continuous spinal, and general
- H. D. ADAMS and N. W. SWINTON—1.30. Operative clinic. Thyroid, stomach, colon, rectum, and biliary tract
- U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1.30. Demonstrations. Anesthesia
- F. H. LANEY, LEWIS M. HERTSHILL, FLEMER C. BARTLE, and H. J. PERKINS—2. Symposium. Thyroid surgery. Subtotal thyroidectomy, diagnosis of hyperthyroidism, diagnosis and treatment of the thyrotoxicosis, complications following thyroid surgery, recent developments in blood saline studies.

#### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

- ELIZABETH E. COWAN—10. Out patient clinics. Gynecology, gynecological, medical, and pediatric
- G. LINCOLN MILLER—10. Pathological presentation. Carcinoma of small intestine, metastases to liver, carcinoma of gastro intestinal tract
- RACHEL L. HARDWICK, BEANCA R. LEE, and MERRY L. FITZMAN—2. Dry clinic. Correlation of electrocardiography with roentgenography in rheumatic heart disease, congenital heart disease, and functional abnormalities, with presentation of cases.

#### NEW ENGLAND MEDICAL CENTER

(Joseph H. Pratt Diagnostic Hospital)

- Staff—1. Dry clinic
- EDWARD T. WHEATLEY—1. Bleeding per ano, illustrated with lantern slides.
- L. H. LAWRENCE—1.30. Manufacturing fact in the female
- K. S. ANDERSON, HENRY H. LEEVER, and WILLIAM M. SHERIDAN—3.30. Recent advances in diagnosis and treatment of cancer of the stomach.

#### PONDVILLE HOSPITAL

- E. M. DALAND, G. W. TAYLOR, H. ROGERS, T. J. ANGLEW, R. H. WALLACE, and associates—9. Operative clinic. Cancer
- Staff—11. Dry clinic.
- F. M. DALAND. End results in cancer of the breast.
- T. J. ANGLEW. Cancer of the mouth, demonstration of cases
- G. W. TAYLOR. Lymph node metastases.
- S. WARREN and associates. Pathological demonstration
- C. E. DEWAS and associates. Roentgen demonstration of bone tumors.

#### ST. ELIZABETH'S HOSPITAL

- Staff—9. Operative and dry clinic:
- JOSEPH STANTON—9. Thyroidectomy.
- MICHAEL E. MCGARTY—9. Bilateral recurrent inguinal hernia
- JOSEPH STANTON—10. Biliary tract operation
- FRANK JACOBSON—10.30. Discussion of subdiaphragmatic and ruptured supraspinatus tendon.
- WILLIAM F. DOLAN—11. Wrist injuries in industry
- MICHAEL E. MCGARTY—11.30. Skin grafts, demonstration of cases

#### SALEM HOSPITAL

- W. G. PHIPPS, DONALD A. NICKERSON, and S. A. WILSON—10. Dry clinic. Uses and abuses of laboratory and roentgenological procedures in abdominal surgery.
- E. L. PRIBORN—11. Prostatic surgery with some newer methods of diagnostic approach.

#### UNITED STATES MARINE HOSPITAL

- RICHIE L. WATSON and associates—8. Operative clinic. Hernioplasty, indirect, direct, and femoral, aponeurotomy, ligation of saphenous vein, hemorrhoidectomy
- RICHIE L. WATSON and associates—1. Dry clinic
- JAMES I. SPENCER. Parasitic appendicitis.
- KENNETH HUGHES. Femoral hernia, a simple operation with report of cases
- RICHIE L. WATSON. Terminal ileitis.
- JOHN A. PRIOR. Rupture of spleen, delayed hemorrhage

#### UNITED STATES NAVAL HOSPITAL

- J. J. A. McFILLIN and staff—9. Operations.

#### Wednesday

#### BETH ISRAEL HOSPITAL

- Staff—9. Dry clinic.
- L. H. NASSON. Pressure treatment of keloids
- J. B. STARR. Prophylaxis of pulmonary embolism by division of femoral vein
- EDWARD HIRSH. Changes in volume of the peritoneal cavity following intercostal nerve paralysis
- C. G. MIXTER. Giant hernia
- ARNOLD STARR. Advanced regional ileitis
- C. G. MIXTER. Transverse ileocolic anastomosis with or without resection for regional ileitis
- Staff—10.30. Operative clinic
- C. G. MIXTER. Intestinal resection
- J. B. STARR. Division of femoral vein for treatment of non fatal pulmonary embolism
- D. D. BERNER. Thyroidectomy
- Staff—1. Dry clinic
- M. D. ALPERT. Obstruction of saphenous vein case
- BENJAMIN ALPERMAN. Food habit
- MAX DAVIS and SAMUEL GILMAN. Venous pressure changes in lower extremities during and after abdominal surgery
- S. B. BEASER. Rare earth anticoagulants

# PRELIMINARY PROGRAM FOR 1941 CLINICAL CONGRESS

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JACOB FINE. Thrombophlebitis and embolism, diagnostic and therapeutic considerations.  
 BENJAMIN ALEXANDER. Polycythemia vera in peripheral vascular disease.  
 B. F. MASSELL and S. B. BEASER. Evaluation of therapy of peripheral vascular disease.  
 JACOB FINE. Adrenal cortical hormones in shock and hemorrhage.

## BOSTON CITY HOSPITAL

Staff—9. Symposium: Cancer.  
 Department of Pathology—9. Splenogenic myeloid metaplasia; argentophil tumors (carcinoid).  
 DR. JOLIFF—9:30. Surgical treatment of myeloma.  
 F. W. O'BRIEN—9:50. Cancer and x-ray therapy.  
 E. A. COONEY—10:20. Carcinoma of breast.  
 A. R. KIMPTON—10:45. Cancer of large intestine.  
 CHARLES LUND—11:10. Cancer of mouth.  
 WILLIAM MORRISON—11:35. Cancer of stomach.  
 Staff—2. Symposium: Thyroid disease.  
 R. C. COCHRANE—2. Tumors of parathyroid, lantern slides.  
 D. D. BERLIN—2:30. Hyperthyroidism in cancer of thyroid.  
 W. T. SALTER—2:50. Graves' disease without hypertension.  
 RICHARD SMITH—3:10. Adenoma of thyroid.  
 Staff—3:30. Symposium: Vitamins in surgery.  
 CHARLES LUND and J. H. CRANDON—3:30. Vitamin C and wound healing.  
 WALTER WEGNER and MERRILL MOORE—4:15. Vitamins in presence of head injuries.  
 DR. MIKELJOHN—4:45. Presentation of cases.  
 Staff—2. Dry clinic:  
 GORDON M. MORRISON—2. Radial nerve injury with fracture of humerus.  
 J. EDWARD FLYNN—2:30. Anatomical and clinical investigations of deep fascial space abscess of hand.  
 T. K. RICHARDS—3:15. Traumatic injuries of the knee joint.  
 A. P. AITKEN—3:45. Epiphyseal separation.  
 ROBERT ULIN—4:30. Clubfeet.

## PETER BENT BRIGHAM HOSPITAL

ELLIOTT C. CUTLER and ROBERT ZOLLINGER—9. Operations: Gastric resections.  
 ELLIOTT C. CUTLER and associates—10. Symposium: Gastric and duodenal ulcer.  
 ELLIOTT C. CUTLER. Indications for surgery.  
 EDWARD S. EMERY, JR. Medical management of bleeding peptic ulcer.  
 MERRILL C. SOSMAN. Significance of prepyloric ulcer.  
 HARRY A. WARREN. Duodenal diverticulum.  
 ROBERT ZOLLINGER. Surgical treatment of severe duodenal ulcer.  
 ELLIOTT C. CUTLER. Results of acute gastroduodenal perforation.  
 CARL W. WALTER—2. Symposium: Aseptic technique.

## CARNEY HOSPITAL

A. McK. FRASER, WILLIAM E. BROWNE, and staff—9. Operative clinic: Gastro-intestinal, biliary tract, thyroid, and hand.  
 Staff—2. Dry clinic:  
 WILLIAM E. BROWNE. Moving picture demonstration and brief description of unusual lesions of arm, forearm, and hand, showing condition present before treatment and end-results. Cases will include xanthomata, glomus tumor, so-called trigger finger contractions, aneurysms in hand, melanotic carcinoma, tendon

suture repair with transplanted segment of vein for covering at site of anastomosis, difference between real and pseudo-neuromata in amputation stumps, ulnar nerve repair, series of median nerve cases, results in a series of cases following radical operation for relief of Dupuytren's contracture with 90 to 100 per cent return of normal function of the hand.  
 DAVID C. DITMORE. Vital tissue staining, its practical application in office and hospital proctology, with report of results in a series of 1000 private patients.  
 W. R. MACAUSLAND. Fracture and dislocation of carpal semilunar bones.  
 HAROLD G. LEE. End-results in lumbosacral fusion; end-results of epicondylar fractures of humerus.  
 A. LEO BRETT. Case presentation of myeloma of 12 years' duration with complete absorption of tenth vertebra.  
 JOHN L. DOHERTY. A simple method of treating fractures of surgical neck of humerus.  
 WILLIAM C. MALONEY. Practical application of clinical laboratory procedures in jaundice.  
 A. McK. FRASER. End-results of gall-bladder surgery.

## CHILDREN'S HOSPITAL

WILLIAM E. LADD and associates—9. Operations.

## DILLON FIELD HOUSE (Soldier's Field, Allston)

AUGUSTUS THORNDIKE, JR., and associates—3. Dry clinic: Athletic injuries. Summary of recent developments in the physiology of physical fatigue.

## FAULKNER HOSPITAL

Staff—8. Operative and dry clinic:  
 E. L. YOUNG, A. R. KIMPTON, F. G. BALCH, H. K. SOWLES, R. F. SHELDON, E. E. O'NEIL, R. S. TITUS, and R. J. HEFFERNAN. Operations.  
 S. C. WIGGIN. Anesthesia exhibits.  
 J. B. HAZARD. Pathological specimens, gross and microscopic.  
 Staff—2. Operative and dry clinic:  
 A. R. KIMPTON—2. Gastric resection.  
 H. K. SOWLES—2:15. Reconstruction operation for hypertrophied breast.  
 E. L. YOUNG—2:30. Stricture of papilla of vater.  
 R. C. COCHRANE—2:45. Parathyroid tumors.  
 Wm. C. QUINBY—3. Importance of water balance in diseases of the prostate.  
 E. E. O'NEIL—3:15. Prevention of pulmonary embolism by ligation and division of femoral vein.  
 R. F. SHELDON—3:30. Local infiltration anesthesia for pelvic delivery.  
 R. J. HEFFERNAN—3:45. Use of progesterin in treatment of habitual and threatened abortion.  
 DR. MALONEY—4. Management of bleeding in jaundice.  
 R. S. TITUS—4:15. Diabetes in pregnancy.  
 DR. STRAUSS—4:30. Importance of vitamins.  
 S. C. WIGGIN—4:45. Anesthesia for complicated surgical cases.

## MALDEN HOSPITAL

LOUIS E. PHANEUF—9. Operation: Vaginal hysterectomy.  
 IRVING J. WALKER—9. Operation: Cholecystectomy.  
 Staff—10. Dry clinic and demonstrations:  
 GORDON D. ATKINSON—10. Urology.  
 RUSSELL F. SULLIVAN—11. Orthopedic surgery.  
 LOUIS E. PHANEUF—11:30. Gynecology.  
 IRVING J. WALKER—12. Ludwig's angina.  
 J. S. ROONEY—12:30. Pathology.  
 KENNETH K. DAY—1. Blood-bank.

## Staff—2 Operative clinic:

- GORDON D. ATKINSON—2 Nephrectomy.  
N. A. GALLAGHER—2.30 Hysterectomy.  
RUSSELL F. SULLIVAN—3.30 Spinal fusion (Hibbs').

## MASSACHUSETTS GENERAL HOSPITAL

- E D CHURCHILL and associates—9 Symposium and clinic: Primary tumors of the lung and esophagus  
D. S. KING—9 Medical aspects of primary carcinoma of the lung  
E D CHURCHILL—9.20 Types of operations and results in carcinoma of the lung  
R. H. SWEET—9.50 Resection of the lung for metastatic sarcoma  
R. H. SWEET—10 Surgical treatment of carcinoma of the lower third of the esophagus and cardiac area of the stomach  
E D CHURCHILL—10.30 Surgical treatment of carcinoma of the upper two thirds of the esophagus  
ROBERT KLOPFER—10.45 Discussion and exhibition of gross pathological specimens.  
Staff—11 Operations  
L. S. McKITTRICK and associates—9 Operative and dry clinic Ulcerative colitis  
C M JONES—9 Medical aspects, diagnosis and treatment  
L. S. McKITTRICK—9.20 Surgical aspects, types of operations and indications  
J D STEWART—9.40 Ileostomy, operative technique, postoperative complications  
RICHARD WARREN—10.10 Late-results after ileostomy, social and economic aspects  
L. S. McKITTRICK—10.30 Colectomy, indications, technique and results  
Staff—10.45 Discussion  
Staff—11. Operations  
H C MARBLE and associates—9 Dry clinic Surgical conditions of the hand  
H C MARBLE Anatomy and examination  
F G BALCH, JR Hand tumors  
EDWARD HAMLIN, JR Injuries to nerves of upper extremity  
BRADFORD CANNON Skin grafts of hand  
A L WATKINS Physiotherapy in reconstruction  
A W REGGIO Occupational therapy in reconstruction  
H C MARBLE Surgical reconstruction  
A W ALLEN and associates—2 Symposium Diseases of the gall bladder and bile ducts  
A W ALLEN—2 Technical considerations of the gall bladder and bile ducts with special reference to morbidity and mortality  
RICHARD WALLACE—2.30 Acute cholecystitis  
J D STEWART—2.50 Obstructive jaundice, liver function, preparation of the patient and after-care  
RICHARD WARREN—3.15 Carcinoma of the gall bladder  
Staff—3.30 Operative clinic Extrahepatic biliary tract  
Staff—2 Symposium Peripheral vascular clinic, obliterative arterial disease  
L. S. McKITTRICK—2 Fundamental considerations, classification, differential diagnosis  
EDWARD HAMLIN, JR—2.15 Thrombo-angitis obliterans Outline of treatment, nerve crushing, mechanical aids, indications for amputation  
H E KENNARD—2.35 Thrombo-angitis obliterans End result study with particular reference to the economic aspect of the disease  
RICHARD WARREN—2.55 Arteriosclerotic gangrene with and without diabetes, indications for and technique of minor amputation

T. C. PRATT—3.10 Arteriosclerotic gangrene with and without diabetes, indications for and technique of supracondylar amputation.

R. H. SMITHWICK—3.30 Lumbar sympathectomy, its rôle in the treatment of obliterative disease, indications for operation and operative technique

Staff—3.50 Discussion

Staff—4 Operative clinic Supracondylar amputation for gangrene, nerve crushing for relief of pain, lumbar sympathectomy.

## MASSACHUSETTS MEMORIAL HOSPITALS

- HOWARD M. CLUTE, CLIFFORD D. HARTY, CHARLES SZIKLAS, FRANK E. BARTON, and HOLLIS L. ALBRIGHT—8 Operative clinic: Thyroid, gall bladder, stomach, and colon.  
ELEANOR FERGUSON, REGINALD HUNT, and M. JEAN BLACK Demonstrations Anesthesia  
GEORGE LEVENE and EEOV G. WISSING—9.30 Demonstration X-ray examination of the rectum and sigmoid with special reference to lateral view.  
Staff—10 Symposium Gastric surgery  
HOWARD M. CLUTE Gastric hemorrhage  
JOHN SPRAGUE End result studies after gastroduodenostomy.  
FRANZ INGLFINGER Miller-Abbott tube in gastrointestinal diagnosis  
THOMAS J. ANGLEM Cancer of the stomach.  
ELEANOR FERGUSON. Anesthesia for upper abdominal surgery  
FRANK E. BARTON—2. Demonstration of transfusion service

## NEW ENGLAND BAPTIST HOSPITAL

- F. H. LAHEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCOCK—9 Operative clinic Thyroid, stomach, colon, and biliary tract  
U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—9 Anesthesia demonstrations Regional, spinal, continuous spinal, and general  
H. D. ADAMS and N. W. SWINTON—1.30 Operative clinic Thyroid, stomach, colon, rectum, and biliary tract  
U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—2.30 Demonstrations Anesthesia

## NEW ENGLAND DEACONESS HOSPITAL

- F. H. LAHEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCOCK—9 Operative clinic Thyroid, stomach, colon, and biliary tract  
U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—9 Anesthesia demonstrations Regional, spinal, continuous spinal, and general  
H. D. ADAMS and N. W. SWINTON—1.30 Operative clinic Thyroid, stomach, colon, rectum, and biliary tract  
U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1.30 Demonstrations Anesthesia  
R. B. CATTELL, N. W. SWINTON, and EVERETT D. KEIPER—2 Dry clinic Diagnosis and treatment of carcinoma of rectum, rectal surgery for benign lesions, diagnosis and treatment of ulcerative colitis  
JOHN NORCROSS Avitaminosis and recent developments in intravenous use of heparin

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

- Staff—10. Out patient clinics Gynecological, skin and allergy, pediatric and well baby  
G. LYNDY MOLLER—10 Pathological demonstration Breast cancer

### NEW ENGLAND MEDICAL CENTER (Joseph H. Pratt Diagnostic Hospital)

#### Staff—9. Dry clinic:

- RICHARD H. OVERHOLT—9. The operability of primary carcinoma of the lung.  
REEVE H. BETTS—9:30. The management of acute pulmonary abscess.  
H. E. MACMAHON—10. Gastric lesions in malignant hypertension.  
S. J. THANNHAUSER—10:30. Liver function tests as an aid to gall-bladder surgery.

### NEWTON HOSPITAL

#### Staff—9. Operative clinic:

- G. KENNETH COONSE—9. A new arthroplasty of the hip.  
LOUIS PILCHER—9. Appendectomy.  
R. I. SMITH—9:30. Thyroidectomy for hyperthyroidism.  
M. P. BRACKETT—9:30. Cholecystectomy.  
D. G. NUTTER—10. Hysterectomy for fibroids.  
E. D. LEONARD—10. Breast amputation.  
HERBERT DUNPHY—11. Skin graft.

#### Staff—2. Dry clinic.

- G. K. COONSE. Diagnosis and treatment of shoulder injuries.  
R. I. SMITH. Tumors of the neck.  
G. D. NUTTER. New apparatus for fractures of the clavicle.  
CHARLES LAMB. Peripheral vascular clinic.  
H. G. DUNPHY. Management of cicatricial contractures due to burns, skin grafting in general.  
E. D. LEONARD. Arterial thrombosis in a young girl.

### ST. ELIZABETH'S HOSPITAL

#### Staff—9. Operative and dry clinic:

- JOHN W. SPELLMAN—9. Surgery of the breast.  
JOSEPH STANTON—9. Gastric surgery.  
EDWARD M. HODGKINS—9. Herniorrhaphy, fascial strips.  
LAWRENCE J. LOUIS—10. Cholecystectomy.  
JOHN G. DOWNING—11. Surgical complications due to fungi. Colored motion picture, "A Clinical and Laboratory Study of Fungous Diseases."  
JOHN W. SPELLMAN—11. Treatment of advanced cancer, demonstration of cases.  
WILLIAM NOONAN—11:45. Spinal anesthesia.

### UNITED STATES NAVAL HOSPITAL

- LAWRENCE J. MCCARTHY and staff—9. Operations.  
JOHN R. MARSHALL and CHARLES H. SWAN—9. Dry clinic. Circulatory diseases of the extremities, case histories.

### Thursday

### BETH ISRAEL HOSPITAL

#### Staff—9. Dry clinic:

- S. S. HANFLIG. Use of traction in treatment of cervical arthritis.  
MYER KARP. Treatment of acute subdeltoid bursitis by needling, novocain and irrigation; mechanics of fracture of surgical neck of humerus, methods of reduction.  
M. H. ROGERS. Manipulation for chronic adhesive bursitis.  
ARMIN KLEIN. Chemotherapy of acute sepsis of bones and joints.  
W. S. ALTMAN. Delayed roentgenological evidence of fracture.  
ARMIN KLEIN. Intervertebral disc, orthopedic aspects.  
W. JASON MIXTER. Intervertebral disc, neurological and surgical aspects.

- DAVID AYMAN. Results of sympathectomy for hypertension.

#### Staff—10:30. Operative clinic:

- R. H. SMITHWICK. Sympathectomy for hypertension.  
W. JASON MIXTER. Removal of intervertebral disc.  
M. H. ROGERS. Arthroscopy of shoulder joint.

#### Staff—2. Dry clinic:

- ALFRED HURWITZ. Sulfanilamide vs. zinc peroxide in the treatment of phagedenic ulcer.  
LOUIS ZETZEL. The Miller-Abbott tube.  
M. D. ALTSCHULE. Effect of abdominal surgery on respiratory dynamics.  
H. L. BLUMGART. The surgical risk in cardiac patients.  
JACOB FINE. Treatment of intestinal distention by sulfaguanidine.  
ARNOLD STARR. Sulfaguanidine for the sterilization of isolated loops of colon.

### BEVERLY HOSPITAL

#### Staff—2. Dry clinic:

- PEER P. JOHNSON. Acute pancreatic disease, its diagnosis and treatment.  
BARNARD P. TODD. Adenoma of the islets of Langerhans.  
RICHARD E. ALT. Abdominal manifestations of renal disease.  
PEER P. JOHNSON and HAMMOND J. DUGAN. Results of deferred operation in acute perforated appendicitis.  
JOSEPH A. CUNNINGHAM. A clinicopathological study of abdominal Hodgkin's disease.

### BOSTON CITY HOSPITAL

- OTTO J. HERMANN and associates—9. Symposium: Low back pain.

#### OTTO J. HERMANN—9. Introduction.

- JOHN T. WILLIAMS—9. Gynecological aspects.  
AUGUSTUS RILEY—9:15. Genito-urinary aspects.  
ROBERT ULIN—9:30. A rational method of routine back examination based on anatomical and physiological factors.  
JOSEPH SHORTELL—9:45. Low back pain with negative x-ray, lumbosacral; sacro-iliac myositis; myositis fasciitis, industrial postural, mechanical findings.  
THOMAS H. PETERSON—10. Coccygodynia fracture of coccyx, conservation vs. surgery in treatment.  
RUSSELL SULLIVAN—10:15. Anatomical abnormalities of fifth lumbar vertebra and lumbosacral joint.  
G. KENNETH COONSE—10:30. Spondylolisthesis, pathology, diagnostic points, role of trauma in its production and treatment.  
A. P. AITKEN—10:45. Fascial contractions.  
MARK H. ROGERS—11. Intervertebral disc problem, orthopedic aspect.  
P. F. BUTLER—11:15. Intervertebral disc problem, x-ray aspect.  
DONALD MUNRO—11:30. Intervertebral disc problem, neurological aspect.  
Staff—2. Operative and dry clinic: Appendicitis, biliary system, and hernia.  
P. S. FOISIE—2. Appendicitis and complications.  
G. W. PAPER—2:30. Incision for appendectomy in extreme obesity.  
F. F. HENDERSON and JOHN MCGOWAN—3. Operative biliary drainage for relief of jaundice, operative care of gall-bladder patient.  
J. J. HEPBURN—3:20. Familial hemolytic jaundice and splenectomy.  
W. R. MORRISON—3:40. Stones of the hepatic ducts subdiaphragmatic abscess.  
CHARLES LAMB—4. Peritoneoscopy with special reference to biliary disease.

- RICHARD SMITH—4 20 Exteriorization of small intestines in strangulated hernia.  
 D. C. GOLDFARB—4 20 Recurrent inguinal hernia.  
 Staff—2. Symposium: Anesthesia, and abdominal surgery  
 T. W. WICKHAM—2. Foci of infection and ulcerative colitis  
 A. R. KEMPTON—2 15. Surgery of large intestine.  
 C. W. McCLURE—2 30. Sigmoidoscopy, kodachrome pictures  
 FRANK MARVIN—2 45. Indications and contra indications for various anesthetics.  
 S. C. WIGGIN—3 Spinal anesthesia.  
 G. C. MOORE—3 15 Intravenous anesthesia  
 P. S. FOSSIE—3 30 Ruptured corpus hemorrhagicum.  
 ALLEN DAVIS—3 45. Calcified cyst of spleen.  
 S. J. MADDOCK—4 High and low intestinal obstruction.  
 ALLEN DAVIS—4 20 Gun shot wounds of abdomen  
 HALSEY B. LODER—4 40. Postoperative treatment.

### PETER BENT BRIGHAM HOSPITAL

- FRANCIS C. NEWTON and J. ENGLEBERT DUNPHY—9 Operations: Colon, rectum and anus  
 ELLIOTT C. CUTLER and associates—10 Symposium. Colon, rectum and anus  
 FRANCIS C. NEWTON. Experiences with cancer of the colon.  
 J. ENGLEBERT DUNPHY. Experiences with anterior resection for cancer of the rectosigmoid  
 ANDREW W. CONTRATTO and THOMAS B. QUIGLEY. Differential diagnosis of gastritis, gastro-enteritis and appendicitis  
 MERRILL C. SOSMAN. The x ray and large bowel surgery  
 EDWARD S. FERRY, JR. Medical diseases of the colon  
 ELLIOTT C. CUTLER. Catatizing enteritis

### CARNEY HOSPITAL

- A. McK. FRASER, WILLIAM E. BROWNE, and staff—9 Operative clinic. Gastro intestinal, biliary tract, thyroid, and hand  
 Staff—2 Dry clinic  
 WILLIAM E. BROWNE. Results of thyroid surgery on a general surgical service during the past 3 years, accuracy of diagnosis and careful pre-operative preparation, types of operative procedure carried out, and results.  
 ROGER C. GRAVES. Management of prostatic obstruction  
 WILSON T. BUDINGTON. Injuries of the ureter  
 CHARLES KICKHAM. Non-calculous obstruction of the urethral pelvic junction  
 ROBERT H. ALDRICH. English experience with war burns  
 JOHN J. TODD. Use of sulfathiazole in surgical infections  
 CHARLES A. ROBINSON. Treatment of varicose ulcer  
 TIMOTHY E. P. LYONS. Results of 3 years' study of carcinoma of the large bowel  
 EDWARD T. WHITNEY. Treatment of fissure in ano

### CHILDREN'S HOSPITAL

- WILLIAM L. LADD and associates—9 Dry clinic. Plastic surgery in children, followed by questions and discussion  
 WILLIAM L. LADD. Harelip and cleft palate  
 DONALD W. MACCOLLUM. Early and late treatment of burns  
 WILLIAM E. LADD. Hands, syndactylism, polydactylism  
 ROBERT F. GROSS. Plastic operations on the anus  
 WILLIAM E. LADD and associates—10 30 Dry clinic, followed by questions and discussions  
 THOMAS H. LAMMAN. Radical treatment of chronic lung suppuration.

- ROBERT E. GROSS. Surgical treatment of patent ductus arteriosus.  
 FRANCIS D. INGRAM. Subdural hematoma, brain tumors in infancy and childhood

### FAULKNER HOSPITAL

- Staff—2 Operative and dry clinic  
 E. G. BRACKETT—2 His operation  
 H. C. MARBLE—2 15 Winger hands  
 HARVEY MORRISON—2 30 Bony block in arthritic knees corrected by operation, motion pictures.  
 OTTO J. HERMAN—2 55. Os calcis fractures, motion pictures  
 DR. NEWTON—3 10 Thoracic surgery  
 JOHN ADAMS—3 25 Hip cases, drilling and pinning  
 H. L. JOHNSON—3 45 Stimulation of fracture repair by embryological regime  
 JOHN HOGAN, C. G. MEXTER, R. H. SMITHWICK, DR. WHITE, E. E. O'NEIL, H. C. MARBLE, and J. S. HODGSON—4 Symposium. Causalgia

### COLLIS P. HUNTINGTON MEMORIAL HOSPITAL

- Staff—2 15 Dry clinic  
 GRANTLEY W. TAYLOR. Choice of treatment in cancer of the oral cavity  
 DAVID WEISBERGER. Changes in the oral mucous membrane due to vitamin deficiency  
 SHIELDS WARREN. Treatment of leukemia by radioactive substances  
 IRA T. NATRANSON. Relation of the hormones to malignant diseases

### MASSACHUSETTS GENERAL HOSPITAL

- A. W. ALLEN and associates—8 Symposium. Duodenal ulcer  
 C. M. JONES and associates—8 Medical considerations  
 A. O. HAMPTON and associates—8 30 Roentgenological diagnosis  
 F. B. BENEDICT—8 50. Gastroscopy, gastritis  
 A. W. ALLEN—9 10 Surgical considerations  
 HOWARD ULFELDER—9 40 Acute perforation  
 C. E. WELCH—10 10 Malfunction of anastomotic stoma and after-care  
 Staff—10 30 Operative clinic  
 V. H. KAZANJIAN—8 Operative and dry clinic. Plastic surgery, presentation of cases operated upon for various deformities  
 L. S. MCKITTRICK and associates—2 Operative and dry clinic. Acute small bowel obstruction  
 RICHARD WARREN—2 Physiological aspects of non strangulation obstruction, cause of death  
 L. S. MCKITTRICK—2 20 Factors influencing mortality rate  
 S. P. SARGIS—2 40 Diagnosis  
 RICHARD WARREN—3 10 Non-operative treatment, practical consideration in the use of the Miller Abbott tube  
 L. S. MCKITTRICK—3 30 Résumé, outline of treatment, results  
 Staff—3 45 Discussion  
 Staff—4 Operations

### MASSACHUSETTS MEMORIAL HOSPITALS

- HOWARD M. CLIFT, CLIFFORD D. HARVEY, CHARLES SZIKLAS, FRANK E. HARTON, and HOLMES L. ALDRICH—8 Operative clinic. Thyroid, gall bladder, stomach and colon  
 ELEANOR FERGUSON, REGINALD HUNT, and M. JEAN BLACK. Demonstrations. Anesthesia

# PRELIMINARY PROGRAM FOR 1941 CLINICAL CONGRESS

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Staff—10. Symposium: Sulfonamides.

CHESTER S. KEEFER. Use of sulfonamides in bacteremia.  
HOWARD M. CLUTE. Use of sulfonamides in peritoneal cavity.

HOLLIS L. ALBRIGHT. Massive infection of abdominal wall and of the extremities, demonstration of cases.  
SAMUEL N. VOSE. Use of sulfonamides in genito-urinary surgery.

LEIGHTON F. JOHNSON. Use of sulfonamides in nose and throat infections.

ARTHUR L. HANRAHAN—10. Operative and dry clinic: Treatment of varicose veins and ulcers.

## NEW ENGLAND BAPTIST HOSPITAL

F. H. LAHEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCOCK—9. Operative clinic: Thyroid, stomach, colon, and biliary tract.

U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—9. Anesthesia demonstrations: Regional, spinal, continuous spinal, and general.

H. D. ADAMS and N. W. SWINTON—1:30. Operative clinic: Thyroid, stomach, colon, rectum, and biliary tract.

U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1:30. Demonstrations: Anesthesia.

## NEW ENGLAND DEACONESS HOSPITAL

F. H. LAHEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCOCK—9. Operative clinic: Thyroid, stomach, colon, and biliary tract.

U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—9. Anesthesia demonstrations: Regional, spinal, continuous spinal, and general.

H. D. ADAMS and N. W. SWINTON—1:30. Operative clinic: Thyroid, stomach, colon, rectum, and biliary tract.

U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1:30. Demonstrations: Anesthesia.

F. H. LAHEY, SARA M. JORDAN, and S. F. MARSHALL—2. Dry clinic: Technique of subtotal and total gastrectomy; medical and surgical management of duodenal and gastric ulcer; treatment of gastrojejunal colic fistula.

HERBERT ADAMS. Diagnosis and treatment of regional ileitis.

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

Staff—10. Out-patient clinics: Gynecological, medical, and pediatric.

G. LINDH MULLER—10. Pathological demonstration: Ovarian tumors.

ELSTIE BROWN and ILIA GALLEANI—2. Dry clinic: Metabolism.

## NEW ENGLAND MEDICAL CENTER (Boston Floating Hospital)

Staff—2. Dry clinic:

RENE H. BETTS and ALFRED WELLES—2. Pulmonary suppuration, treatment of empyema in children.

RICHARD WAGNER and W. S. LEVENSON—2:30. Endocrinology and surgery.

FRANCIS McDONALD and R. G. FREEMAN—3. Appraisal of the host, nutrition, personality.

FRANCIS McDONALD, W. S. LEVENSON, NICHOLAS WERTHESEN, and H. E. MACMAHON—3:30. Case of adrenal dysfunction.

H. E. CHAMPELIN—4. Genito-urinary surgery in children.

W. A. MACCOLL—4:30. Tonsils and adenoids, indications for removal.

## PALMER MEMORIAL HOSPITAL

Staff—9. Symposium: Carcinoma of the rectum and anus. L. S. MCKITTRICK. Choice of operation in cases of carcinoma of the rectum.

W. F. LEADBETTER. Urological complications after excision of the rectum.

C. C. FRANSEEN. Use of electrocoagulation and radium implantation in poor-risk cases of carcinoma of the rectum.

J. H. MARKS. X-ray therapy of carcinoma of the rectum.

R. H. SWEET. End-results of treatment of carcinoma of the rectum and anal canal.

## ST. ELIZABETH'S HOSPITAL

Staff—9. Operative and dry clinic:

JOSEPH STANTON—9. Cholecystectomy.

JOHN SPELLMAN—9. Resection of large bowel.

JOSEPH STANTON—10. Hysterectomy.

FRANCIS JANTZEN—10. Herniorrhaphy.

WILLIAM SANTORO—11. Cholecystectomy.

MARTIN H. SPELLMAN—11. Herniorrhaphy.

ROGER T. DOYLE—11. Presentation of cases.

JOHN F. CASEY—11:45. The use of sulfonamides in general surgery.

## UNITED STATES NAVAL HOSPITAL

JOSEPH B. LOGUE—9. Operations.

LAWRENCE J. MCCARTHY and FRANKLIN G. BALCH, JR.—9. Operative and dry clinic: Gastro-intestinal diseases, partial gastrectomy for pyloric obstruction; synopsis of case histories.

## Friday

## BETH ISRAEL HOSPITAL

Staff—9. Dry clinic:

C. G. MIXTER. Results of surgery of colon neoplasms classified according to extent of lesion.

L. E. BARRON. Pitfalls in diagnosis of carcinoma of stomach, observations in 300 cases.

C. G. MIXTER. Results of surgery of gastric neoplasms classified according to extent of lesion.

I. T. NATHANSON. Surgical management of lymph nodes in cancer surgery.

K. PRESSER. Differential diagnosis of gastric ulcer by radiography.

JACOB FINE—10:30. Operation: Colon resection.

C. G. MIXTER—10:30. Operation: Gastric resection.

Staff—2. Dry clinic:

A. M. SELIGMAN. Vitamin K<sub>1</sub> in treatment of hypoprothrombinemia in infants.

J. J. MICHAELS and ETHEL COHEN. Psychiatric considerations in surgical patients.

B. E. F. RISEMAN. The surgical treatment of angina pectoris.

S. A. ROBINS. Diagnosis of non-calcified dermoid cysts.

A. M. SELIGMAN. Carcinogenic agents.

H. L. CABITT. Surgical management of pulmonary tuberculosis.

AARON THURMAN. Thoracic esophageal diverticulum.

NAAMAN STEINBERG. Injection treatment of hemorrhoids.

## BOSTON CITY HOSPITAL

Staff—2. Dry clinic:

C. G. SHERB—2. Chemotherapy in general peritonitis.

MAXWELL FINLAND—2:30. Chemotherapy in surgery.

R. H. ALDEICH—3:15. The dymital treatment of burns with especial reference to shock.

H. G. DUNPHY—4:15. "Z" plastics in burns.



## PETER BENT BRIGHAM HOSPITAL

- ELLIOTT C. CUTLER and ROBERT ZOLLINGER—9. Operations: Cholecystectomy, choledochostomy.  
 ELLIOTT C. CUTLER and associates—10. Symposium: Surgical diseases of the biliary tract  
 ELLIOTT C. CUTLER. Biliary calculus, technique of surgical therapy.  
 MERRILL C. SOSMAN. Upright films of the gall bladder as an aid in the diagnosis of cholelithiasis.  
 ROBERT ZOLLINGER. Acute cholecystitis.  
 THOMAS B. QUICKLY. Surgery of the biliary tract in the aged  
 WILLIAM A. DAVIS. Clinical use of vitamin K in surgery of the biliary tract.  
 EDWARD S. EMERY, JR. Medical treatment after cholecystectomy.  
 ELLIOTT C. CUTLER and associates—2. Symposium: Surgical treatment of hyperthyroidism  
 ELLIOTT C. CUTLER. The domain of thyroid surgery.  
 SAMUEL A. LEVINE. Pre-operative and postoperative treatment of severe thyrocardiacs.  
 MARSHALL N. FULTON. Recurrent hyperthyroidism  
 J. ENGBERT DUNPHY. Use of silk in surgery of the thyroid.  
 HARRY B. FRIEDGOOD. Role of the pituitary hormone in thyrotoxicosis  
 ELLIOTT C. CUTLER. Technique of thyroidectomy.

## CARNEY HOSPITAL

- A. McK. FRASER, WILLIAM E. BROWNE, and staff—9. Operative clinic: Gastro-intestinal, biliary tract, thyroid, and hand.

## CHILDREN'S HOSPITAL

- WILLIAM E. LADD and associates—9. Operations.

## MASSACHUSETTS GENERAL HOSPITAL

- F. D. CHURCHILL, OLIVER COPE and associates—9. Symposium: Hyperparathyroidism  
 J. C. AUB—9. Physiology of the parathyroid glands  
 CUTLER ALBRIGHT—9.20. Clinical aspects of hyperparathyroidism.  
 TRACY B. MALLORY—9.30. Pathology of the parathyroid glands.  
 OLIVER COPE—10. Surgical treatment of hyperparathyroidism.  
 F. A. SIMONE—10.35. Renal complications of hyperparathyroidism  
 Staff—11. Operative clinic  
 Staff—2. Symposium: Peripheral vascular disease, acute venous thrombosis in veins of lower extremities, pulmonary embolism.  
 RICHARD WARREN—2. Fundamental considerations of thrombus formation, clinical manifestations, diagnosis and treatment  
 H. H. FAXON—2.20. Pulmonary embolism, its relation to venous thrombosis  
 RICHARD WARREN—2.45. The use of heparin in the prevention of pulmonary emboli  
 C. E. WELCH and C. E. MCGAHEY—3. Venography, indications, technique, results  
 H. H. FAXON—3.15. Exploration and division of the femoral vein, indications and operative technique  
 C. E. WELCH—3.35. Results, early and late, after division of the femoral vein  
 Staff—3.50. Discussion

- H. H. FAXON, C. E. WELCH, and RICHARD WARREN—4. Operative clinic.

## MASSACHUSETTS MEMORIAL HOSPITALS

- HOWARD M. CLUTE, CLIFFORD D. HARVEY, CHARLES SEIKLAS, FRANK E. BARTON, and HOLMES L. ALBRIGHT—8. Operative clinic: Thyroid, gall bladder, stomach, and colon.  
 ELEANOR FERGUSON, REGINALD HUNT, and M. JEAN BLACK. Demonstrations: Anesthesia.  
 REGINALD HUNT—10.30. Dry clinic: Spinal headaches, preliminary report.  
 M. JEAN BLACK. Relative efficiency of different methods of oxygen therapy.

## NEW ENGLAND BAPTIST HOSPITAL

- F. H. LAHEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCOCK—9. Operative clinic: Thyroid, stomach, colon, and biliary tract  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—9. Anesthesia demonstrations: Regional, spinal, continuous spinal, and general  
 H. D. ADAMS and N. W. SWINTON—1.30. Operative clinic: Thyroid, stomach, colon, rectum, and biliary tract  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1.30. Demonstrations: Anesthesia

## NEW ENGLAND DEACONESS HOSPITAL

- F. H. LAHEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCOCK—9. Operative clinic: Thyroid, stomach, colon, and biliary tract.  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—9. Anesthesia demonstration: Regional, spinal, continuous spinal and general.  
 H. D. ADAMS and N. W. SWINTON—1.30. Operative clinic: Thyroid, stomach, colon, rectum, and biliary tract  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1.30. Demonstration: Anesthesia

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

- Staff—10. Out patient clinics: Gynecological, ophthalmological, vascular, and pediatric (cardiac)

## PALMER MEMORIAL HOSPITAL

- Staff—2. Symposium: Diabetic gangrene  
 H. F. ROOT. Medical aspects.  
 L. S. MCKITTRICK. Principles of surgical treatment, classification of lesions, conservative methods  
 T. C. PRATT. Indications for and technique of minor amputation  
 L. S. MCKITTRICK. Indications for and technique of major amputation  
 T. C. PRATT. End result study of 100 patients after supracondylar amputation for gangrene  
 L. S. MCKITTRICK and T. C. PRATT—2. Operations: Supracondylar amputations for gangrene

## ST ELIZABETH'S HOSPITAL

- JOSEPH STANTON and staff—9. Operations.

## SALI M HOSPITAL

- Staff—10. Clinical pathological conference

## UNITED STATES NAVAL HOSPITAL

- CHARLES H. SWAN—9. Operations.

## OBSTETRICS AND GYNECOLOGY

Tuesday

## BOSTON CITY HOSPITAL

Staff—2. Symposium: Pregnancy, the physiological and pathological aspects.

GEORGE R. MINOT and EUGENE L. LOZNER—2. The hemorrhagic diatheses complicating pregnancy.

FREDERICK J. LYNCH—2:30. Treatment of miscarriage.

FREDERICK PARKER, JR.—3. Pathology of toxemia of pregnancy with especial reference to changes in the placenta.

CARMEL R. ALDEN—3:30. Disorders of the urinary tract encountered in obstetrics.

BENEDICT F. BOLAND—4. Hormonal relationship between the kidneys and toxemia of pregnancy.

MAXWELL FINLAND—4:20. Pneumonia in pregnancy.

## BOSTON LYING-IN HOSPITAL

Staff—10. Operative and dry clinic:

CHARLES A. JANEWAY. Treatment of puerperal sepsis with sulfanilamide and immune transfusions.

CLEMENT A. SMITH. Quantitative measurements of anesthesia and anoxia produced in mother and infant by obstetrical anesthetics.

## CARNEY HOSPITAL

LOUIS E. PHANEUF and staff—9. Operative clinic.

Staff—2. Dry clinic:

LOUIS E. PHANEUF. Manchester operation in management of uterine prolapse.

R. J. HEFFERNAN. Conservative management of premature separation of the placenta.

ROGER C. GRAVES and LOUIS E. PHANEUF. Management of difficult vesicovaginal fistula.

II. EDWARD MACMAHON. Biopsy of uterine cervix from the standpoint of the pathologist.

MAURICE O. BELSON. Uterine hemorrhage; technique of uterovaginal tamponade.

EDMUND L. CAREY. Analysis of breech deliveries at the Carney Hospital during the last 10 years.

WILLIAM C. MALONEY. Abnormal capillary fragility in the newborn.

## FREE HOSPITAL FOR WOMEN

JOHN ROCK and SIDNEY C. GRAVES—8. Gynecological operations.

Staff—9. Symposium: Carcinoma of the cervix.

FRANK A. PEMBERTON—9. Radium application. Demonstration of radium applicators.

FRANK A. PEMBERTON and RICHARD DRESSER—9:20. Present methods of radium and x-ray treatment.

ARTHUR T. HERTIG and PAUL A. YOUNG—9:40. Diagnosis of early carcinoma, clinical and pathological.

GEORGE VAN S. SMITH—10:40. Complications and treatment.

PAUL A. YOUNG—11. Management of the urological complications.

GEORGE VAN S. SMITH—11:20. Results and summary.

PAUL A. YOUNG—11:45. Hysterectomy for early carcinoma of the cervix.

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

LUTITIA DOUGLAS ADAMS, BLANCHE L. ATWOOD, ILIA GALIFANI, and GRACE E. ROCHFORD—9. Operations.

MARJORIE WOODMAN—2. Obstetrical analgesia.

ESTHER E. BARTLETT—2. Demonstration: Pudendal and parasacral blocks in obstetrical anesthesia.

## PALMER MEMORIAL HOSPITAL

G. A. LELAND, JR. and C. J. SWAN—2. Symposium: Treatment of carcinoma of the cervix.

## ST. ELIZABETH'S HOSPITAL

Staff—9. Demonstration: Technique of normal delivery.

FREDERICK L. GOOD and staff—10. Operations.

Wednesday

## BOSTON CITY HOSPITAL

Staff—9. Dry clinic:

Speaker to be announced—9. Anesthesia and analgesia with special reference to spinal and intravenous anesthesia.

DR. REGINALD and R. D. MARGESON—9:30. Placenta previa in patients previously delivered by low transverse cesarean section.

FREDERICK L. GOOD—10. Physiology of the lower uterine segment.

DANIEL J. MCSWEENEY—10:30. Radiographic pelvimetry.

F. W. O'BRIEN—11. Results in treatment of carcinoma of the uterus in the tumor clinic of a general hospital.

FREDERICK PARKER, JR., and JOHN T. WILLIAMS—11:30. Pathology of so-called fibrosis of the uterus.

## BOSTON LYING-IN HOSPITAL

Staff—2. Dry clinic:

MEINOLPH V. KAPPIUS. The rôle of soft tissue x-ray technique in the diagnosis of placenta previa.

ROBERT N. RUTHERFORD. Interpretation of bleeding in the first trimester of pregnancy as shown by endometrial biopsies.

ARTHUR T. HERTIG. Pathological ova, chief cause of spontaneous abortion.

ROBERT H. BARKER. Determination of cephalopelvic disproportion by Thoms method of roentgenometry.

## CARNEY HOSPITAL

LOUIS E. PHANEUF and staff—9. Operative clinic.

## FREE HOSPITAL FOR WOMEN

EDWARD B. SHEEHAN and CHRISTOPHER J. DUNCAN—8. Gynecological operations.

Staff—9. Operative and dry clinic: Carcinoma of the endometrium.

FRANK A. PEMBERTON—9. Hysterectomy for carcinoma of the endometrium.

FRANK A. PEMBERTON and RICHARD DRESSER—10. Present methods of treatment, surgery, radium and x-ray.

ARTHUR T. HERTIG—10:30. Pathology and diagnosis of early carcinoma.

GEORGE VAN S. SMITH—11. Results and summary.

PAUL A. YOUNG—11:30. Biopsy and cauterization of the cervix in ambulatory patients.

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

Staff—9. Operations.

MARJORIE WOODMAN—9:30. Obstetrical ward rounds.

MARJORIE WOODMAN—2. Obstetrical analgesia.

ESTHER E. BARTLETT—2. Demonstration: Parasacral and pudendal blocks in obstetrical anesthesia.

## PONDVILLE HOSPITAL

JOE V. MEIGS, LANGDON PARSONS, and associates—9. Operative clinic: Wertheim operation for cancer of the



## THORACIC SURGERY

*Monday*

## MASSACHUSETTS MEMORIAL HOSPITALS

JOHN W. STRIEDER and W. W. WOODRUFF (Saranac Lake, New York)—2. Symposium: Thoracic surgery. Suppurative pericarditis, colored moving pictures; lobectomy for bronchiectasis; tuberculous empyema.

## NEW ENGLAND BAPTIST HOSPITAL

H. D. ADAMS—1:30. Operations.

## NEW ENGLAND DEACONESS HOSPITAL

H. D. ADAMS—2. Operations.

Staff—2. Operative clinic: Non-tuberculous thoracic surgery.

*Tuesday*

## NEW ENGLAND BAPTIST HOSPITAL

H. D. ADAMS—1:30. Operations.

## NEW ENGLAND DEACONESS HOSPITAL

H. D. ADAMS—1:30. Operations.

Staff—2. Dry clinic: Symposium on total pneumonectomy.

REEVE H. BETTS. Determination of operability in primary carcinoma of the lung.

SHIELDS WARREN. Pathology of lung cancer.

RICHARD H. OVERHOLT. Exploratory thoracotomy in suspected malignancy.

BERT H. COTTON. Use of sulfathiazole in pulmonary resection.

ANDREW YEOMANS. Physiological observations made at time of pulmonary resection.

PHILLIP SCHULTZ. Problems of anesthesia in pneumonectomy.

HOWARD ROOT. Medical aspects of postoperative management.

Staff. Presentation of cases treated by pneumonectomy for cancer, tuberculosis, bronchiectasis, and cystic disease.

*Wednesday*

## MASSACHUSETTS MEMORIAL HOSPITALS

JOHN W. STRIEDER—2. Operative clinic: Lobectomy for bronchiectasis; thoracoplasty for pulmonary tuberculosis.

## NEW ENGLAND BAPTIST HOSPITAL

H. D. ADAMS—1:30. Operations.

## NEW ENGLAND DEACONESS HOSPITAL

H. D. ADAMS—1:30. Operations.

*Thursday*

## MASSACHUSETTS GENERAL HOSPITAL

E. D. CHURCHILL and associates—2. Operative and dry clinic: Suppurative lesions of the lung.

D. S. KING—2. Medical aspects of bronchiectasis, prognosis of untreated cases.

L. DAVENPORT—2:20. Technique of bronchography and anatomy of bronchial tree.

E. D. CHURCHILL—2:40. The surgical treatment of bronchiectasis.

R. H. SWEET—3. Surgical treatment of lung abscess, results.

E. D. CHURCHILL—3:30. Lobectomy and pneumonectomy in lung abscess.

ROBERT KLOPSTOCK—3:45. Discussion and exhibition of gross pathological specimens.

## NEW ENGLAND BAPTIST HOSPITAL

H. D. ADAMS—1:30. Operations.

*Friday*

## BOSTON CITY HOSPITAL

Staff—9. Operative and dry clinic:

J. W. STRIEDER—9. Colored motion pictures of suppurative pericarditis; result of modern method of treatment of putrid empyema; lobectomy for bronchiectasis.

HORACE BINNEY—9:45. Methods and results of treatment of pulmonary tuberculosis.

S. J. G. NOWAK—10:45. Experimental pulmonary embolus.

DR. SHULTZ—11:30. Intratracheal anesthesia for thoracic surgery.

## NEW ENGLAND DEACONESS HOSPITAL

RICHARD H. OVERHOLT and R. H. BETTS—10. Dry clinic.

H. D. ADAMS—1:30. Operations.

Staff—2. Dry clinic: Symposium on total pneumonectomy.

REEVE H. BETTS. Determination of operability in primary carcinoma of the lung.

SHIELDS WARREN. Pathology of lung cancer.

RICHARD H. OVERHOLT. Exploratory thoracotomy in suspected malignancy.

BERT H. COTTON. Use of sulfathiazole in pulmonary resection.

ANDREW YEOMANS. Physiological observations made at time of pulmonary resection.

PHILLIP SCHULTZ. Problems of anesthesia in pneumonectomy.

HOWARD ROOT. Medical aspects of postoperative management.

Staff. Presentation of cases treated by pneumonectomy for cancer, tuberculosis, bronchiectasis, and cystic disease.

## NEW ENGLAND BAPTIST HOSPITAL

H. D. ADAMS—1:30. Operations.

## ORTHOPEDIC SURGERY

## Tuesday

## CHILDREN'S HOSPITAL

FRANK R. OBER and associates—9 Operations

## NEW ENGLAND BAPTIST HOSPITAL

G. E. HAGGART and J. W. TOOMEY, JR.—9 Operations

## NEW ENGLAND DIACONESS HOSPITAL

G. E. HAGGART and J. W. TOOMEY, JR.—9 Operations

## Wednesday

## ROBERT BRECK BRIGHAM HOSPITAL

Staff—9 Operative Clinic.

JOHN G. KERNS Arthroplasty of elbow

ROBERT J. JOPLIN Posterior capsularplasty of knee for flexion deformity

WILLIAM A. ELLISTON Osteotomy for malum coxae senilis

Staff—2 Symposium End results in correction of arthritic deformities

LORING T. SWAIM Treatment of spinal arthritis.

JOHN G. KERNS Correction of contractures of the knee

ROBERT J. JOPLIN End results in arthroplasties of elbow.

JOHN A. REIDY Arthroplasties of knee

WILLIAM A. ELLISTON Treatment of osteo-arthritis of hip

## CARNEY HOSPITAL

W. R. MACALUSLAND and staff 9 Operative clinic

## CHILDREN'S HOSPITAL

Staff—9 Dry clinic

WILLIAM A. ELLISTON Study in bone growth and resection of the epiphyseal plate

L. P. J. McDERMOTT Equalization of leg length; leg lengthening

PAUL W. HUGENBERGER Tuberculosis of bone

ALBERT H. BREWSTER Arthrodesis of the foot in spastic paralysis.

Staff—11 Symposium Infantile paralysis, operative treatment, round table discussion

## MASSACHUSETTS MEMORIAL HOSPITALS

LOUIS G. HOWARD, KENNETH CHRISTOPHER, and WILLIAM ELLISTON—9 Operative clinic Spinal fusion, hip reconstruction with vitallium cup.

## NEW ENGLAND BAPTIST HOSPITAL

G. E. HAGGART and J. W. TOOMEY, JR.—9 Operations

## NEW ENGLAND DIACONESS HOSPITAL

G. E. HAGGART and J. W. TOOMEY, JR.—9 Operations

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

MIRIAM G. KATZELL—9 Operations.

MIRIAM G. KATZELL—10 Dry clinic Arthritis, fractures, x rays of pathological bone conditions, clubfoot demonstration

## ST ELIZABETH'S HOSPITAL

THOMAS F. BRODERICK—9 Spinal fusion

THOMAS F. BRODERICK—11.30 Dry clinic Motion pictures of author's technique of spinal fusion

## UNITED STATES NAVAL HOSPITAL

THOMAS H. PETERSON—9 Dry clinic. Shoulder injuries, discussion of case histories; x ray findings

## Thursday

## CHILDREN'S HOSPITAL.

FRANK R. OBER and associates—9 Operations

## FAULKNER HOSPITAL

E. G. BRACKETT, H. C. MARBLE, G. M. MORRISON, J. L. DOHERTY, J. D. ADAMS, and OTTO J. HERMANN—8 Operative clinic

HARVEY MORRISON X-ray demonstrations

## MASSACHUSETTS GENERAL HOSPITAL

M. N. SMITH PETERSEN and associates—2 Operative and dry clinic

M. N. SMITH-PETERSEN, ARMIN KLEIN, J. S. BARR, and PAUL L. NORTON—2 Operations

WILLIAM A. ROGERS—2 Fractures and fracture dislocations of the cervical spine, results of operative treatment

GEORGE VAN GORDE Amputations

E. F. CAVE Fractures of the carpal scaphoid, results of bone graft

O. SHREVEY STAPLES Effect on the knee joint of pansastragalar arthrodesis

OTTO I. ALFRANG, CARROLL B. LARSON, and M. N. SMITH PETERSEN Surgical procedures for relief of deformities arising from rheumatoid arthritis

WALTER BAUER Discussion

## MASSACHUSETTS MEMORIAL HOSPITALS

LOUIS G. HOWARD, ALBERT B. FERGUSON, and THOMAS J. ANGLIM—9 Symposium Discussion of malignant bone tumors

## NEW ENGLAND BAPTIST HOSPITAL

G. E. HAGGART and J. W. TOOMEY, JR.—9 Operations

## NEW ENGLAND DIACONESS HOSPITAL

G. E. HAGGART and J. W. TOOMEY, JR.—9 Operations

## ST ELIZABETH'S HOSPITAL

THOMAS F. BRODERICK and staff—9 Operations

## Friday

## CARNEY HOSPITAL

W. R. MACALUSLAND and staff—9 Operative clinic.

## CHILDREN'S HOSPITAL

Staff—9 Dry clinic followed by round table discussion

MIRIAM G. KATZELL—9 Early treatment of clubfeet

ROBERT H. MORRIS—10 Treatment of difficult clubfeet

FRANK R. OBER—9.30 Treatment of congenital elevation of the scapula

WILLIAM T. GREEN—10.30 Osteochondritis dissecans

MYRON G. KARP—10.45 Fractures about the elbow in childhood

Staff—11.15 Congenital malformations

## MASSACHUSETTS GENERAL HOSPITAL

M. N. SMITH PETERSEN and associates—8.30 Operative and dry clinic

- G. W. VANGORDER, W. A. ROGERS, and E. F. CAVE—8:30. Operations.  
 ARMIN KLEIN, JOHN A. REIDY, and ROBERT J. JOPLIN—9. Slipped upper femoral epiphysis, results of operative and non-operative treatment.  
 JOSEPH S. BARR. Spinal fusion, frequency of pseudarthrosis.  
 M. N. SMITH-PETERSEN, CARROLL E. LARSON, and OTTO E. AUFRANC. Arthroplasty of the hip, results.

NEW ENGLAND BAPTIST HOSPITAL  
 G. E. HAGGART and J. W. TOUMEX, JR.—9. Operations.

NEW ENGLAND DEACONESS HOSPITAL  
 G. E. HAGGART and J. W. TOUMEX, JR.—9. Operations.

UNITED STATES NAVAL HOSPITAL  
 THOMAS H. PETERSON—9. Operations.

## GENITO-URINARY SURGERY

### Tuesday

#### BETH ISRAEL HOSPITAL

Staff—9. Dry clinic:

- E. G. CRABTREE. Pre-operative preparation of prostatic cases.  
 G. C. PRATHER and M. L. BRODNY. Accessory bladder pathology in prostatic cases.  
 G. C. PRATHER and MORTIMER REICH. Accessory renal pathology in prostatic cases.  
 E. G. CRABTREE. Summary of 12 years' experience in prostatic surgery.  
 G. C. PRATHER. Results of contact therapy for bladder tumors.  
 E. G. CRABTREE—10:45. Operation: Bladder tumor, contact radiation therapy.

Staff—2. Dry clinic:

- E. L. PRIEN. Adaptation of the Tratner hydrophorograph for bladder studies.  
 ABRAHAM ZIMMERMAN. Bladder atonies.  
 J. H. LIPTON. Bladder atonies as demonstrated by the Tratner hydrophorograph.  
 S. R. MUELLNER. Testosterone effect on bladder tone; diabetic atony of the bladder.  
 B. E. GREENBERG. Value of cholinergic and adrenergic drugs in bladder atonies.  
 H. A. KONTOFF. Rate of recovery of bladder after relief of obstruction.  
 S. R. MUELLNER. Stress incontinence in the female.  
 E. L. PRIEN. Crystallography of the sulfonamide drugs.

#### CHILDREN'S HOSPITAL

- WILLIAM E. LADD and associates—9. Dry clinic: Diseases of the genito-urinary tract in infancy and childhood, followed by questions and discussion.  
 WILLIAM E. LADD. Embryoma of the kidney (Wilms' tumor).  
 ROBERT E. GROSS. Surgical treatment of malformations.  
 THOMAS H. LANMAN. Extrophy and epispadias.

#### MASSACHUSETTS MEMORIAL HOSPITALS

Staff—9. Operative clinic:

- M. J. HAHN—9. Pyelotomy for stone.  
 DAVID B. STEARNS—10. Suprapubic prostatectomy.  
 SAMUEL N. VOSE—11. Perineal prostatectomy.

#### NEW ENGLAND BAPTIST HOSPITAL

E. E. EWERT and VERNON S. DICK—9. Operations.

#### NEW ENGLAND DEACONESS HOSPITAL

E. E. EWERT and VERNON S. DICK—9. Operations.

#### ST. ELIZABETH'S HOSPITAL

EDWARD J. O'BRIEN and associates—10. Operations.

### Wednesday

#### MASSACHUSETTS GENERAL HOSPITAL

- G. G. SMITH and associates—9. Operative and dry clinic: Staff—9. Operations.  
 F. H. COLBY—10:30. Genito-urinary tuberculosis.  
 RICHARD CHUTE—10:50. Results of treatment with estrogenic substances in prostatic hypertrophy.  
 S. B. KELLEY—11:10. Complications of transurethral resection.  
 LORANDE WOODRUFF—11:40. The female urethra.  
 G. G. SMITH and associates—2. Operative and dry clinic: Staff—2. Operations.  
 G. G. SMITH—3:30. Treatment of prostatic cancer.  
 ARTHUR WILLETS—3:50. Chronic prostatitis.  
 WYLAND LEADBETTER—4:10. Renal arteriography.  
 JOHN GENS—4:30. Urological endocrinology.

#### MASSACHUSETTS MEMORIAL HOSPITALS

Staff—9. Symposium: Obstructing prostate.

- CLYDE L. DEMING (New Haven, Connecticut). Functional end-results following perineal prostatectomy.  
 EDWARD N. COOK (Rochester, Minnesota). Pre-operative preparation for transurethral prostatectomy.  
 SAMUEL N. VOSE. Selection of operative procedure.  
 JOSEPH F. MCCARTHY (New York). Technical aspects of prostatic resection with commentary on pharmacological adjuvants.

#### NEW ENGLAND BAPTIST HOSPITAL

E. E. EWERT and VERNON S. DICK—9. Operations.

#### NEW ENGLAND DEACONESS HOSPITAL

HARVARD H. CRABTREE—9. Operations.

E. E. EWERT and VERNON S. DICK—9. Operations.

#### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

SUSANNAH FRIEDMAN—2. Dry clinic: End-results of pyelitis of pregnancy.

#### NEWTON HOSPITAL

E. G. CRABTREE, G. C. PRATHER, and E. L. PRIEN—9. Operations.

Staff—2. Dry clinic:

- E. L. PRIEN. Analysis of calcifications and crystals in renal tissue.  
 G. C. PRATHER. Cystin stone and cystinuria.  
 E. G. CRABTREE. Block dissections for renal tumor and cancer of the bladder.  
 G. C. PRATHER. Calyceal diverticula.  
 E. L. PRIEN. Multiple recurrent stones, palliation.  
 E. G. CRABTREE. Uretero-nephrectomy.  
 G. C. PRATHER. Graphic evidence of upper urinary dilatation with lower urinary obstruction.

## PONDVILLE HOSPITAL

- ROGER C. GRAVES and associates—9 Operative clinic:  
Carcinoma of the bladder.  
Staff—11. Dry clinic  
ROGER C. GRAVES Carcinoma of the bladder  
CHARLES C. J. KICKHAM Urological complications in  
carcinoma of the rectum and colon  
WESTON T. BUDDINGTON Urological complications in  
carcinoma of the cervix

## Thursday

## BETH ISRAEL HOSPITAL

- Staff—9 Dry clinic  
E. L. PRIEN A new method for stone analysis  
D. B. STEARNS Parathyroid disease and urinary lithiasis  
G. C. PRATHER Roentgenology of the kidney at operation  
B. E. GREENBERG Use of cholinergic and adrenergic medication for ureteral stone passage  
H. A. KONTOFF Hospital statistics on urinary lithiasis  
J. H. LITTON Clearance of infection in stone cases after operation  
D. B. STEARNS Diagnosis of calyceal calcifications  
H. A. KONTOFF Renal tumor statistics of the hospital  
Demonstration of surgical specimens of renal tumors with pyelographic and microscopic data  
E. G. CRABTREE—11 Operation Excision of renal tumor  
Staff—2 Dry clinic  
M. L. BRODNY Fractional phylography.  
J. H. LITTON Sulfonamide drugs in surgical wounds and postoperative infections  
B. E. GREENBERG Methylene blue treatment for tuberculosis of the bladder  
E. L. PRIEN Renal injury from sulfathiazole and sulfa pyridine, nature of the lesion  
D. B. STEARNS Undescended testicle, age groups  
M. L. BRODNY Urological study of enuresis cases  
DR. FISHMAN Denervation of the kidney, end-results of 200 cases  
B. E. GREENBERG Organization and function of a sterility clinic  
NATHAN CHASET Hypertensive disease in urology

## BOSTON CITY HOSPITAL

- Staff—9 Operative and dry clinic  
H. H. HOWARD—9 Epidermoid carcinoma of the penis  
GEORGE C. PRATHER—9 25 Stricture of the urethra  
S. R. MUELLNER—9 50 Newer concepts of urinary extravasation  
G. D. ATANSON—10 15 Scrotal plastics after idiopathic gangrene  
W. F. HOLTHAM—10 40 Treatment of gonorrheal urethritis with sulfathiazole  
J. A. BETH—11 25 Removal of calculi from lower ureter by the vaginal route, report of 2 cases  
F. G. STODOLAN—11 25 Fracture of the penis, case report. Anatomical study of remnants of prostate tissue in the prostatic bed following enucleation  
AUGUSTUS RILEY—11 40 Hemangioma of kidney, case report

## PETER BENT BRIGHAM HOSPITAL

- WILLIAM C. QUINBY and associates—2 Symposium  
J. HARTWELL HARRISON The diagnosis and treatment of common injuries of the urinary tract

- GEORGE AUSTEN. A correlation of the clinical aspects and pathology of the fused renal mass.  
G. PHILIP GRABFIELD Renal blood flow  
F. ANTHONY SIMEONE Experimental hypertension  
WILLIAM C. QUINBY. A critical evaluation of prostatic surgery in recent years

## CARNEY HOSPITAL

- ROGER C. GRAVES and staff—9 Operative clinic.

## MASSACHUSETTS GENERAL HOSPITAL

- G. G. SMITH and associates—9 Operative and dry clinic  
Staff—9 Operations  
HOWARD SUEY—10 30 Solution of urinary calculi  
RICHARD CRUTE—10 50 Problems in the treatment of urinary calculi  
F. H. COLBY—11 15 Deep x ray therapy in cancer of the bladder  
S. B. KELLEY—11 40 Ureterostomy versus nephrostomy

## NEW ENGLAND BAPTIST HOSPITAL

- E. E. EWERT and VERNON S. DICK—9 Operations.

## NEW ENGLAND DEACONESS HOSPITAL

- E. E. EWERT and VERNON S. DICK—9 Operations.

## UNITED STATES NAVAL HOSPITAL

- NICHOLAS G. SCARCELLO—9 Dry clinic Presentation of urological cases with histories and x-ray findings

## Friday

## MASSACHUSETTS GENERAL HOSPITAL

- R. H. SMITHWICK and associates—2 Symposium Surgery of non nephritic hypertension  
ROBERT S. PALMER Statement of the problem  
BENJAMIN CASTLEMAN Renal pathology  
JOHN S. TALBOT Renal physiology  
RICHARD CRUTE Urological factors  
R. H. SMITHWICK. Modification of abnormal physiology by sympathectomy

## MASSACHUSETTS MEMORIAL HOSPITALS

- Staff—9 Dry clinic  
DAVID B. STEARNS Prostatovesiculitis simulating upper urinary tract symptomatology  
SAMUEL N. VOSE Radical prostatectomy for cancer of prostate  
FRANK MORSE, JR. Congenital bladder neck obstruction in male children.  
M. F. HAHN, JR. Review of urinary calculus at Massachusetts Memorial Hospitals for past 15 years

## NEW ENGLAND BAPTIST HOSPITAL

- E. E. EWERT and VERNON S. DICK—9 Operations

## NEW ENGLAND DEACONESS HOSPITAL

- E. E. EWERT and VERNON S. DICK—9 Operations

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

- G. LINDA MULLER—10 Pathological demonstration  
Congenital abnormalities of the kidney, nephrolithiasis

## NEUROSURGERY

*Monday*

## MASSACHUSETTS GENERAL HOSPITAL

- J. C. WHITE and associates—2. Symposium: Neurological surgery.  
 J. C. WHITE and J. J. MICHELSEN—2. Operations.  
 W. J. MIXTER—4. Electro-encephalographic control of anticonvulsant therapy.  
 C. S. KUBIC and A. O. HAMPTON—4. Removal of lipiodol by lumbar puncture.  
 J. C. WHITE—4. Effect of anesthesia on volume of brain.

## NEW ENGLAND BAPTIST HOSPITAL

GILBERT HORRAX—1:30. Operations.

## NEW ENGLAND DEACONESS HOSPITAL

GILBERT HORRAX—1:30. Operations.

*Tuesday*

## MASSACHUSETTS GENERAL HOSPITAL

- J. C. WHITE and associates—9. Operative and dry clinic:  
 W. J. MIXTER and J. S. HODGSON—9. Operations.  
 J. C. WHITE—11. Presentation of operative results in angina pectoris and extrapyramidal tremors.  
 J. J. MICHELSEN—11. Treatment of torticollis by alcohol injection of cervical muscles.  
 J. C. WHITE and associates—2. Dry clinic:  
 W. J. MIXTER. Protrusion of nucleus pulposus in cervical spine.  
 J. S. HODGSON. Experience with cerebellar hemangiomas (Lindau's disease).  
 J. J. MICHELSEN. Subdural abscess.  
 W. H. SWEET. New methods for measurement of blood flow.  
 J. C. WHITE. Spinothalamic tractotomy in the medulla.

## NEW ENGLAND BAPTIST HOSPITAL

J. L. POPPEN—9. Operations.  
 GILBERT HORRAX—1:30. Operations.

## NEW ENGLAND DEACONESS HOSPITAL

J. L. POPPEN—9. Operations.  
 GILBERT HORRAX—1:30. Operations.

*Wednesday*

## BOSTON CITY HOSPITAL

- DONALD MUNRO and associates—9. Symposium: Injuries of the central nervous system and allied conditions.  
 DONALD MUNRO—9. Treatment of compound fracture of the skull, a study of 175 cases.  
 WALTER WEGNER—9:20. Concomitant cerebral tumors and craniocerebral injuries.  
 TIMOTHY LEARY—9:40. Pathology of craniocerebral injuries, with demonstration of specimens.  
 DONALD MUNRO—10:40. Study of 300 consecutive intracranial subdural hematomas.  
 WALTER WEGNER—11. Care of bone damage in cervical spinal cord injuries.  
 DONALD MUNRO—11:15. Present-day tidal drainage of the urinary bladder.  
 C. W. ELKINS—11:30. Two-needle oxygen spinograms with improved visualization of the spinal subarachnoid space.

- DONALD MUNRO—11:45. Study of end-results in 130 cases of all levels of spinal cord injury.  
 DONALD MUNRO—12:10. Spinothalamic tractotomy in the medulla, intradural differential section of the sensory root of the fifth cranial nerve and other procedures of use in dealing with intractable pain in the head, face, mouth, neck, and arms.  
 DONALD MUNRO—12:20. Differential diagnosis and treatment of Ménière's disease and aural vertigo.  
 DONALD MUNRO—12:30. Prophylaxis and treatment of pressure bed-sores.

## NEW ENGLAND BAPTIST HOSPITAL

J. L. POPPEN—9. Operations.  
 GILBERT HORRAX—1:30. Operations.

## NEW ENGLAND DEACONESS HOSPITAL

J. L. POPPEN—9. Operations.  
 GILBERT HORRAX—1:30. Operations.

*Thursday*

## CHILDREN'S HOSPITAL

- F. D. INGRAHAM and associates—9. Symposium: Neurological surgery of children.  
 F. D. INGRAHAM—9. Neurosurgical problems of infancy and childhood.  
 BRONSON CROTHERS—9:30. Definition of recovery in terms of growth and development.  
 F. D. INGRAHAM—9:45. Congenital anomalies requiring surgical treatment.  
 F. D. INGRAHAM—10:15. Technical aids in neurosurgery of infancy and childhood.  
 F. D. INGRAHAM—10:30. Reliability of encephalography in infancy.  
 BRONSON CROTHERS—10:45. Presentation of cases.  
 SYDNEY FARBER—11. Pathological aspects of neurosurgery.  
 F. D. INGRAHAM—11:30. Excision of premotor cortex for athetosis.  
 F. D. INGRAHAM—12. Subdural hematoma.

## NEW ENGLAND BAPTIST HOSPITAL

J. L. POPPEN—9. Operations.  
 GILBERT HORRAX—1:30. Operations.

## NEW ENGLAND DEACONESS HOSPITAL

GILBERT HORRAX and associates—2. Operations:  
 GILBERT HORRAX. Ventriculogram and craniotomy for brain tumor.  
 J. L. POPPEN. Herniated intervertebral disc.

*Friday*

## NEW ENGLAND BAPTIST HOSPITAL

J. L. POPPEN—9. Operations.  
 GILBERT HORRAX—1:30. Operations.

## NEW ENGLAND DEACONESS HOSPITAL

GILBERT HORRAX and associates—9. Dry clinic:  
 J. L. POPPEN—9. Results in herniated intervertebral discs, operations with and without fusions.  
 J. L. POPPEN—9:30. Platybasia demonstration.  
 GILBERT HORRAX—10. Experiences and results in brain tumors for the last 8 years.



## FRACTURES AND OTHER TRAUMAS

## Tuesday

## BOSTON CITY HOSPITAL

OTTO J. HERMANN and associates—9 Symposium: Fractures of the ankle

OTTO J. HERMANN. Introduction

GORDON M. MORRISON. Simple unilateral ankle injuries with fracture.

JOSEPH BURNETT, G. G. BAILEY, JOSEPH SHORTELL, and RUSSELL SULLIVAN. Complicated ankle fractures, bilateral, following Cotton's therapeutical ankle classifications. Slides, charts, individual cases, and apparatus illustrating various points.

## Thursday

## BEVERLY HOSPITAL

Staff—9. Operative and dry clinic

PEER P. JOHNSON. Interesting fractures, end results

JOHN D. ADAMS. Injuries to hip joint, drilling of femoral neck in dislocation of hip joint

RICHARD E. ALT. Open reduction in fractures and dislocations

PAUL E. TIVNAN and JOSEPH A. CUNNINGHAM. Clinicopathological conference on bone tumors

JACOB H. FINE. Demonstration of recently constructed operating amphitheater eliminating fire and explosion hazards

## Friday

## BOSTON CITY HOSPITAL

Staff—9. Symposium. Fractures of the hip

NEWTON C. BROWDER—9. Intracapsular fractures of the hip

RUSSELL SULLIVAN—9.30. Hip fractures, cases of operative reduction and internal fixation.

OTTO J. HERMANN—10. Painful ununited hip fractures

THOMAS H. PETERSON—10.30. Posterior fusion of the hip

A. A. THIBODEAU—11. Slipped femoral epiphysis

JAMES W. SEVER—11.30. Presentation of cases

DR. WISE (of New York)—11.45. Presentation of autopsy specimens of nailed fractured hips

## MASSACHUSETTS GENERAL HOSPITAL

A. W. REGGIO, A. W. ALLEN, M. N. SMITH PETERSEN, H. C. MARBLE, G. W. VANDORDER, and associates—2

Dry clinic.

Staff—2. Fracture rounds, presentation of current cases with open discussion

Staff—3.30. End result clinic, presentation of follow up cases with open discussion of problems

## UNITED STATES MARINE HOSPITAL

RICHIE L. WAUGH and associates—8. Operative clinic. Internal derangement of knee joint, bunion, closed treatment, double pan method, fracture both bones of leg, open treatment using vitallium plate

RICHIE L. WAUGH and associates—1. Dry clinic

RICHIE L. WAUGH. Skeletal traction and countertraction methods applicable to ordinary extension splints in the treatment of fractures of lower extremity

THOMAS A. HATHCOCK. Use of vitallium in fractures

RICHIE L. WAUGH. Injuries of the wrist

## OTORHINOLARYNGOLOGY

## Monday

## NEW ENGLAND BAPTIST HOSPITAL

F. D. LATHROP—1.30. Operations

## NEW ENGLAND DEACONESS HOSPITAL

W. B. HOOVER and F. D. LATHROP—2.30. Local anesthesia in tonsillectomy, adenoidectomy, lingual tonsillectomy, and excision of lateral pharyngeal bands, septum, sinus surgery—Caldwell Luc, external frontal, intranasal, plastic procedures, external nose.

## NEW ENGLAND MEDICAL CENTER

(Boston Dispensary—Joseph H. Pratt Diagnostic Clinic)

GEORGE KELEMEN—2. Pathogenesis of traumatic cholesteatoma, lantern slides, surgery of the tonsil after middle-ear; pathways of infection in the ear, lantern slides.

PHILIP E. MELTZER—2. Surgical anatomy of the temporal bone.

## Tuesday

## BOSTON CITY HOSPITAL

Staff—9. Dry clinic

E. J. MONAHAN—9.30. A method of the extirpation of bronchial cysts.

OSCAR HIRSCH—9.50. Cysts of pituitary body.

LOUIS M. FREEDMAN—10.10. Bronchoscopic treatment of pulmonary atelectasis

CHESTER R. MILLS—10.30. Osteomyelitis of the frontal bones.

BENJAMIN RISEMAN—10.50. Gumma of nasopharynx and lung.

SAMUEL W. GARTIN—11.10. Treatment of fractures of the jaw.

PHILIP E. A. SHERIDAN, CHARLES DEWOLFE and FREDERICK HEIMLUCK—11.30. Presentation of cases

## CHILDREN'S HOSPITAL

Staff—9.30. Dry clinic:

CHARLES F. FERGUSON. Acute laryngotracheal bronchitis, report and statistical study of 40 cases

C. G. FLAKE. Congenital anomalies of the tracheal bronchial tract, treatment of choanal atresia

C. G. FLAKE and CHARLES F. FERGUSON. Chemotherapy in upper respiratory infections of children

## MASSACHUSETTS EYE AND EAR INFIRMARY

Staff—2.30. Dry clinic.

A. S. MACMILLAN. Interpretation of sinus x rays.

L. G. RICHARDS. Problems in bronchoscopy.

C. T. PORTER. Orbital abscess, diagnosis and treatment

L. A. SCHAAL. Cancer of the nose and sinuses

## MASSACHUSETTS MEMORIAL HOSPITALS

Staff—2. Operative clinic.

HAROLD L. BABCOCK. Mastoidectomy.



## OPHTHALMOLOGY

*Monday*

## MASSACHUSETTS EYE AND EAR INFIRMARY

F. H. VERHOEFF and WILLIAM P. BEETHAM—2 15 Dry Clinic. Cataract surgery

*Tuesday*

## BOSTON CITY HOSPITAL

JAMES J. REGAN and staff—9 Symposium. Abnormal fundi.

## UNITED STATES NAVAL HOSPITAL

JAMES J. REGAN—9 Demonstrations of technique used in flight physical examinations, with discussions of United States Naval requirements  
VIRGIL G. CASTEN—10 30 Operations.

## MASSACHUSETTS EYE AND EAR INFIRMARY

PAUL A. CHANDLER, FRED S. THORNE, TRAYVE GUNDERSEN, and PAUL G. HAIRE—9 Operations.

WILLIAM P. BEETHAM—9 Demonstration. Slit lamp.  
PAUL A. CHANDLER—2 15. Dry clinic. Glaucoma, indications for operation

SAMUEL T. CLARKE—3 15 Dry clinic. Goniotomy; medical treatment of glaucoma.

*Wednesday*

## MASSACHUSETTS EYE AND EAR INFIRMARY

WILLIAM P. BEETHAM, SAMUEL H. WILKINS, BRENDAN D. LFAHEY, and DAVID G. COGAN—9 Operations

GARRETT L. SULLIVAN—9 Demonstration. Perimetry  
E. B. DUNPHY—2 15 Dry clinic. Strabismus, orthoptic training

VIRGIL G. CASTEN—3 15 Dry clinic. Strabismus, operative treatment

## MASSACHUSETTS MEMORIAL HOSPITALS

WILLIAM D. ROWLAND—9 30 Dry clinic

*Thursday*

## BOSTON CITY HOSPITAL

JAMES J. REGAN and staff—9 Operations.

## CARNEY HOSPITAL

GEORGE GAGLIARDI—2. Dry clinic. Suture and cataract extraction.

LEROY FORD—2 Dry clinic. Orbital abscess in children  
SAMUEL T. CLARKE—2. Contact lenses

## MASSACHUSETTS EYE AND EAR INFIRMARY

EDWIN B. GOODALL, RALPH H. REGGLES, MERRILL J. KING, and HERMAN GROSSMAN—9 Operations.

VIRGIL G. CASTEN—9 Demonstration. Neuro-ophthalmology.

MERRILL J. KING—2 15 Dry clinic. Retinal separation  
BRENDAN D. LEAHEY—3 15 Dry clinic. Keratoplasty.

## MASSACHUSETTS MEMORIAL HOSPITALS

WILLIAM D. ROWLAND, JOSEPH J. SKIRBALL, EDWARD L. PERRY, and RALPH H. HOPKINS—2 Operative clinic  
Cataract, glaucoma, and muscles

## ST. ELIZABETH'S HOSPITAL

HUGH DONAHUE—10 Operations. Cataract extraction, decompression operation for primary glaucoma

*Friday*

## CARNEY HOSPITAL

SAMUEL T. CLARKE and staff—9 Operative clinic.

## MASSACHUSETTS EYE AND EAR INFIRMARY

BENJAMIN SACHS and JOHN G. JENNINGS—9 Operations  
Staff—9 Demonstrations

SAMUEL T. CLARKE. Gonioscopy  
T. L. TERRY—2 15 Dry clinic and lantern demonstrations of pathological specimens

V. H. KAZANJIAN—3 15. Dry clinic. Ophthalmoplastic surgery.

## MASSACHUSETTS EYE AND EAR INFIRMARY

## SCIENTIFIC EXHIBIT

*Daily*

T. L. TERRY. Pathological laboratory open for inspection  
DAVID G. COGAN. Howe laboratory and library open for inspection

# SURGERY

## GYNECOLOGY AND OBSTETRICS

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### CHRONIC PERICARDIAL DISEASE

#### Report of Twenty-Eight Cases of Constrictive Pericarditis

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C. SIDNEY BURWELL, M.D., Boston, Massachusetts

**I**NFECTION of the pericardial cavity may be followed by complete or partial obliteration of the sac, by extension of the reaction to the mediastinum and other surrounding structures with resulting adhesions, or simply by a variable number of benign adhesions which unite the pericardium and epicardium. This latter condition is usually undiscovered during life since it rarely if ever results in untoward symptoms. Because of these facts, simple asymptomatic adhesions will be dismissed without further consideration. Even generalized union of the epicardium and pericardium if nonconstricting may produce no significant disturbance of cardiac function.

The condition in which there are adhesions that connect the heart and pericardium to the surrounding structures is known as mediastinopericarditis. It is believed that most cases follow rheumatic fever. Some instances of mediastinopericarditis are of interest from the viewpoint of surgical therapy, and they will be discussed subsequently.

More interesting because of its frequency and better response to operative treatment is the condition in which the heart is compressed

From the Department of Surgery of Vanderbilt University, Nashville, and the Department of Medicine, Harvard Medical School.

by dense scar tissue, usually known as chronic constrictive pericarditis. The major portion of this paper will be devoted to a consideration of this condition. Before beginning this, for the sake of completeness, one should mention the fact that there is an occasional patient without pericardial adhesions or scars in whom symptoms referable to the heart result from displacement of this organ by a chronic inflammatory process of the lung and pleura. It may be necessary to perform a thoracoplasty in order to allow the heart and great vessels to return to the normal position.

Constrictive pericarditis and mediastinopericarditis will be considered in the order named.

#### CHRONIC CONSTRICTIVE PERICARDITIS

The treatment by operation of patients with chronic constrictive pericarditis constitutes one of the most gratifying chapters in the history of surgery of the heart. The subject is not new but it is only in recent years that the frequency of both the disease and its response to operation have been appreciated. This is demonstrated by the fact that Churchill (23) in 1929 was able to find in the literature the reports of only 37 cases in which operation had been performed. Since that

time, pericardiectomy for chronic constrictive pericarditis has been carried out on a combined total of more than 60 patients in the Massachusetts General Hospital in Boston, in the Lakeside Hospital in Cleveland, and in the Vanderbilt Hospital in Nashville. The diagnosis has been made in each of these clinics on a good many other patients on whom operation was not performed for various reasons. The reports in the literature indicate an increasing number of patients in whom the diagnosis is made and the scar is removed. For example, quite recently, the results of 7 such operations were reported by Heuer and 9 were described by Harrington.

#### DEFINITION

Chronic constrictive pericarditis may be defined as a thickening and contraction of the pericardium or epicardium or both to such an extent that there is interference with the normal action of the heart. It is generally agreed that the ability of the heart to dilate to the usual extent and hence to receive the normal quantity of blood during diastole is markedly diminished. It is likely that the emptying of the heart is interfered with to a lesser degree. The pericardial sac may be completely obliterated or there may be areas in which the two layers are not adherent. The pericardium may or may not exhibit areas of calcification; usually it does not. Small collections of fluid may be trapped between the thickened epicardium and pericardium. Important disease of the heart itself is rare except for atrophy of the myocardium in advanced cases. These structural changes by interfering with the movements of the heart and blood lead to a recognizable clinical picture which will be described subsequently. A photograph of an autopsy specimen is shown in Figure 1 and a photomicrograph of a section of this is given in Figure 2.

#### REVIEW

According to White (57), the first clear cut description of pericarditis was given by Lower in 1669. The condition was recognized by Lancisi in 1728, by Morgagni in 1761, and by Laennec in 1819. Hope in 1839 expressed the belief that endocarditis coexists with pericar-

ditis in the immense majority of cases and reported that he had never examined an autopsy specimen of complete adhesion of the pericardium without finding enlargement of the heart. He wrote,

"Pericarditis, both acute and chronic, and especially that originating in acute rheumatism, frequently terminates in adhesion of the pericardium. Lancisi, Vieussens, Meckel, Senac, Corvisart, and more strongly than all Morgagni, are of opinion that, with a complete and ultimate adhesion, the patient cannot live in a state of health. I know not how it is that Laennec and Bertrin and Bouillard have formed an opposite opinion. The former states that he had opened a great number of subjects so affected, who had never complained of any derangement in the circulation or respiration, whence he infers that adhesion often does not in any respect interfere with the exercise of functions. Bouillard, in his later work, adheres though with a slight qualification, to the same opinion."

Hope continues in stating that his own experience is entirely opposed to this doctrine.

"Nor has the additional experience of seven years, since the preceding sentence was written, afforded me reason to alter my opinion. I have never seen an individual with complete adhesion of the pericardium enjoying the most flourishing health."

Hope apparently realized that tuberculosis may be the cause of pericarditis.

"In scrofulous and phthisical individuals, tubercles are sometimes developed in the false membranes of pericarditis and according to Laennec, this may cause the acute to pass into the chronic state, as frequently happens in the case of pleuritic and peritoneal false membranes."

Chevers in 1842 disagreed with Hope's statements concerning the frequent association of adhesive pericarditis and cardiac enlargement. It was his impression that Hope's views were correct only in those instances in which there was disease of heart valves as well as adhesive pericarditis. When the valves were healthy, Chevers observed a general diminution in the size of the heart and a contraction of its cavities. He described 4 patients with the autopsy findings in each case. All clearly had constrictive pericarditis. None had an enlarged heart. In 2 of them, tubercles were described. He states:

"It will be observed that in the cases which I have cited there is no evidence of the pericardial adhesions being owing to rheumatic inflammation: on the con-



Fig. 1. This picture of an autopsy specimen shows the greatly thickened pericardium—epicardium overlying the left ventricle. It measured 3 centimeters in thickness at the base of the heart. The obliterated pericardial cavity is represented by the linear necrotic zone which is visible in some areas. The process was tuberculous in origin and activity was still present. Patient died less than 24 hours after entering the hospital.

trary, the adhesion of the lungs to the pericardium, in several, renders it probable that it depended upon severe disease of the idiopathic kind."

That Chevers had a good understanding of the disease is illustrated by the following:

"The principal cause of dangerous symptoms in cases of the above description appears to arise from the occurrence of gradual contraction in the layer of adhesive matter which has been deposited around the heart, compressing its muscular tissue, and embarrassing its systolic and diastolic movements, but more particularly the latter. Under these circumstances, the circulation seems, after a time, in great measure to adapt itself to the encumbered condition of the heart. The ventricles, having become diminished in capacity, make up for this loss by the rapidity of their contractions (hence the small and rapid pulse, noticed in three of the above cases): while the main arteries, if not already diseased, adapt themselves to the dimensions of the cavities from which they arise. . . . The heart had, doubtless, for a long time continued to become more and more compressed, weakened, and embarrassed, by the gradual contraction of the adventitious structure

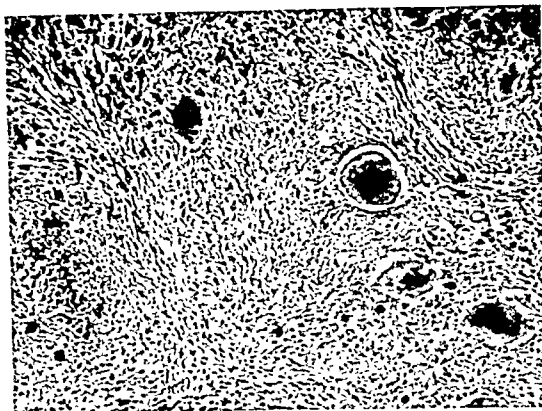


Fig. 2. Photomicrograph of scar shown in Figure 1. Many giant cells are present.  $\times 100$ .

which surrounded it: distention of the great veins and abdominal viscera had necessarily followed; and the resulting anasarca, ascites, and effusion of serum into the pleura, in the second and third case, and also into the air cells of the lungs in the second, must have added still more to the obstruction with which the already almost powerless heart had to contend."

Concerning pericarditis associated with valvular disease, Chevers stated:

"It is evident, that if morbid contraction of any part of the valvular apparatus of the heart occurs coincidentally with the first adhesion of the pericardial surfaces, the cavities behind the obstacle will have begun to suffer consequent dilation and thickening long before the adhesions have become so contracted as to exert much pressure upon their walls. And I am not prepared to maintain that a simply adherent state of the pericardium could materially check the occurrence of dilatation, should valvular contraction be set up at any subsequent period; but I must repeat, that it does not appear to me that we are at present in possession of the slightest definite proof that mere adhesion of its surface has any tendency to produce either dilatation or thickening of the heart."

Chevers found that there were recorded between 1835 and 1842, in the Museum Inspection Books, accounts of 47 cases in which adhesions of long standing were found uniting the pericardial surfaces. In 30 of these, the adhesions were general.

"The fact, that in nearly one half of the cases of partial adhesion the heart retained its ordinary dimensions, while in the remainder there was sufficient valvular disease to account for any enlargement that was present, would tend to prove that partial adhesion of the pericardial surfaces is not more liable to



Fig 3 Rheumatic pericarditis, to be contrasted with the greater amount of exudation and fibrosis in tuberculous pericarditis in Figure 4  $\times 5$



Fig 4 Tuberculous constrictive pericarditis with activity  $\times 5$

produce hypertrophy with dilatation than is the more complete form of the disease."

Wilks in 1871 agreed with Chevers in his conception of constrictive pericarditis. He remarked:

"I give six examples of cases where death was due apparently to adherent pericardium, and in looking through our post-mortem records I find that I might have added two or three more from every annual return. Therefore the condition cannot be regarded as being a rare one. A perusal of these cases would almost incline me to offer the proposition that in a well marked case of disease with cardiac symptoms in young persons without any valvular bruit pericardial adhesions may be fairly expected. In older persons, of course, we should look rather to degeneration of muscular tissue."

In 1873, Kussmaul called attention to a decrease in pulse amplitude in inspiration. Pick in 1896 gave a clear description of the differentiation of primary cirrhosis of the liver and chronic pericarditis. The disease is frequently designated by his name but this usage can hardly be considered correct in view of the previous excellent descriptions. The probable reason for the attachment of Pick's name to this condition is that it was at the time of his description that Weill and Delorme suggested resection of the pericardium for the relief of chronic constrictive pericarditis. Carl Beck in 1901, made a similar suggestion. This operation was first attempted by Henle in 1907 on a patient of Volhard's. The first successful result was reported by Rehn in 1920, the operation having been performed a number of years previously.

At the time that Delorme was pleading for the employment of surgery in the treatment of constrictive pericarditis, a great scientist, the founder of modern light therapy, Niels Ryberg Finsen, suffered from the disease. A recent consideration of his illness is given by Hugo Roesler. Finsen became ill at the age of 23 and was partially incapacitated during the remaining 21 years of his life. The findings on physical examination included ascites, pleural effusion, enlarged liver and spleen, normal sized heart, slight peripheral edema, cyanosis at times, and increased venous pulsations in the neck. He wished to avoid abdominal paracenteses and he reduced the rate of accumulation of ascites by low fluid intake, magnesia and ammonium chloride. He investigated extensively on himself the problem of water and salt metabolism and he placed himself on a low salt intake. His death occurred the year following the receipt of the Nobel prize. At the autopsy (performed at his request), extensive pericardial disease with calcification and an absence of valvular disease were found. The history of pulmonary hemorrhages suggests that the disease was tuberculous in origin.

The description of constrictive pericarditis by Volhard and Schmieden in 1923 is classic. It represents the greatest advance in the understanding of the mechanism of the disease since the description by Chevers in 1842. Volhard made a number of important points. He pointed out that simple adhesions produce no symptoms while the thickened adhesions cause symptoms because the heart loses its capacity



Fig. 5. Infra-red photograph of patient of Stewart and Heuer. a, Preoperative photograph; b, 3 weeks after pericardectomy; c, 4 months later; d, 10 months after pericardectomy; e, 17 months after pericardectomy. The

to dilate sufficiently to carry out its work. *Accretio cordis* or mediastinopericarditis, in which the primary disturbance is in systole, was differentiated from *concretio cordis* or constrictive pericarditis, and it was stated that there are intermediate types. Volhard stressed the disproportion between the maximal signs of peripheral congestion and the minimal signs of abnormality on examining the heart itself. The venous pressure was measured directly and the small heart in the presence of venous distention was commented upon. Volhard said that the neck veins collapse somewhat in both systole and diastole. He considered the increased pressure in neck veins as a most important point in differentiating the disease from cirrhosis. Seven patients with constrictive pericarditis were described by Volhard and good results were obtained in the 2 operated upon by Schmieden.

Youmans in 1926 reported 2 instances of calcification of the pericardium diagnosed during life and considered 94 collected cases in which the condition was found at autopsy. Collier incised in several directions the thickened pericardium of one of their patients. Definite improvement resulted despite the fact that no scar was removed.

progressive decrease in the prominence of the veins, the disappearance of the ascites and the change in shape of the chest are to be noted. (From Stewart, H. J., and Heuer, G. J. New York St. J. Med., 1939, 39: 2183.)

Churchill (23) in 1929 reported the first successful resection of the pericardium for constrictive pericarditis in the United States and stimulated a still growing interest in the problem of the disease in this country. The second successful result was reported shortly afterward by Bigger (8).

Beck and Griswold (5) reported in 1930 the successful production of constrictive pericarditis in dogs by introducing Dakin's solution into the pericardial cavity. The picture is practically identical with that observed in patients. This method not only permits the obtaining of additional information concerning the mechanics of the disease but also allows one to secure added practice with the performance of a very delicate operative procedure which is carried out for the relief of the condition.

There has been careful analysis of a group of patients by White (57), admirably recorded in the St. Cyr lecture and there has been a series of studies on the circulatory dynamics of patients by Beck and Griswold (5), Burwell and Strayhorn (21), Burwell and Flickinger (19), Burwell and Blalock (18), Stewart, and others. An important review of the subject was presented by Schur in 1934.





Fig 6 Photograph of autopsy specimen showing changes in inferior vena cava and hepatic veins. The viscera are seen from behind. The lungs have been removed and the aorta and inferior vena cava opened posteriorly. On the right the inferior vena cava can be seen passing from below upward to the "pars hepatica," where there is marked constriction, and into the right auricle of the heart. The two large, most inferior openings are the renal veins. The hepatic veins are of small size and there are thrombi in some of them. Two large hepatic veins opening above the constriction show narrowing almost to the point of occlusion. Note the greatly dilated veins on the dome of the diaphragm at the right.

#### PHYSIOLOGICAL CONSIDERATIONS

Many of the physiological mechanisms that are important in the manifestations and treatment of this condition were understood and described by Cohnheim 50 years ago as a result of his studies on the effects of fluid in the pericardial cavity. In considering the signs and symptoms of constrictive pericarditis, it is interesting that most of them are dependent upon two changes in the dynamics of the circulation. Studies that were carried out by Burwell, Strayhorn, Flickinger, Bowerman and others (18) have shown clearly that there are two simple mechanical disturbances behind the symptoms and signs which distinguish this condition. First, there is a diminution of the amount of blood pumped by the heart per minute and per beat and an inability to increase the output per beat. This diminution leads to weakness, fatigue, tachycardia, low pulse pressure, and a limited tolerance for exertion. The second mechanical disturbance

is the increase in systemic venous pressure. The term "systemic" is used because the pressure in the pulmonary veins in patients cannot be measured and because various findings indicate that the congestion is more severe in the systemic than in the pulmonary area. Quite aside from any other change, an increase in venous pressure in itself can lead to venous distention, to engorgement of the liver, to the formation of peripheral edema, to nosebleeds, and to the transudation of fluid into the pleural and peritoneal cavities. The spinal fluid pressure rises with the venous. It has been found in experimental animals (12) that the lymphatic pressure also rises with the venous pressure. The alterations in the circulation were described by Heuer and Stewart as follows:

"Briefly, it was found in this group of patients that the arteriovenous oxygen difference was increased, the venous pressure elevated, and the circulation time prolonged, while the cardiac output per minute, the stroke volume and the cardiac index (cardiac output in liters per square meter of body surface per minute) were diminished."

Thus, the alterations in constrictive pericarditis include changes in the venous pressure which are similar to those in congestive heart failure and changes in the cardiac output and blood pressure which are somewhat similar to those observed in patients in shock. In the latter condition, however, the veins are usually

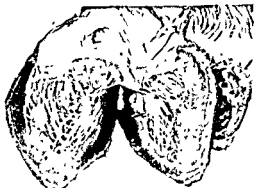


Fig 7 Autopsy specimen, tuberculous pericarditis without fluid but with activity. This is the stage of the disease in which it has been necessary to operate upon most of our patients. Evidences of compression were not very marked in this patient.

collapsed, in sharp contrast to the distended veins seen in constrictive pericarditis.

Perhaps the alteration which is most responsible for the production of signs and symptoms is the marked increase in venous pressure. It has been observed by Burwell and Blalock (18) that marked improvement may follow a reduction in the venous pressure with little or no increase in the output of the heart. Usually, however, the output of the heart increases following operation as the venous pressure falls and it is impossible to place the blame accurately. The dyspnea that most patients with constrictive pericarditis experience on slight exertion is presumably due to the inability of the heart to increase its output adequately, and thus resembles the dyspnea suffered by normal persons after severe exercise. The edema, on the other hand, apparently is not due to the diminished cardiac output but rather in the main to the elevated venous pressure. This is suggested by the distribution of the edema, which is observed chiefly in the areas drained by the systemic veins (in which the pressure is much above the normal), while the volume flow of blood is necessarily reduced to the same degree in both peripheral and pulmonary circuits.

Schur is of the opinion that the extracardiac factors are important in constrictive pericarditis. He states if the only element were back pressure from the heart that the signs and symptoms would be identical with those encountered in any type of heart failure. There is marked interference with venous return in all cases of constrictive pericarditis and Schur believes this to be particularly true of the hepatoportal system. He says that the broadening of the hepatic vein orifices during inspiration does not take place in the presence of dense adhesions of the heart, diaphragm, and neighboring structures. He agrees with Schmieden and Fischer (49) that systole of the heart is also interfered with rather seriously. The heart is fixed at the base and at the apex, and it cannot shorten sufficiently to perform its work effectively. It appears, as has been stated, that the disabilities of constrictive pericarditis arise chiefly from the fact that the heart cannot dilate to a normal extent during diastole. One is also impressed by the disturb-

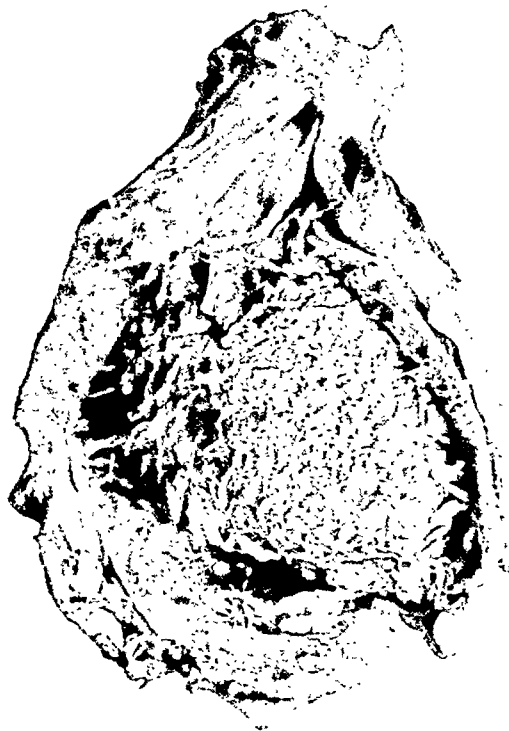


Fig. 8. Autopsy specimen, tuberculous pericarditis, small amount of fluid, shaggy exudate. Little can be accomplished by operating in this stage of the disease.

ance of contraction and emptying which must be associated with an almost unyielding scar closely attached to the heart, and it seems likely that the heart could not put out a normal volume of blood per beat even if it could receive it.

#### ETIOLOGY

It is our contention, on the basis of evidence to be presented, that most instances of constrictive pericarditis result from infection with tuberculosis. It is impossible to be certain as to the etiology of many of the reported cases of constrictive pericarditis since a clear differentiation is not made in the majority of the articles between mediastinopericarditis, constrictive pericarditis, and simple nonconstricting adhesions between the pericardium and epicardium. In addition, if the scar is healed, microscopic study will not usually reveal the etiology of the disease.

Wells found adherent pericarditis of various degrees in 57 of 1,048 autopsies. Of these 57

cases, 8 were due to rheumatic infection, 6 were frankly tuberculous, and 43 were of undetermined cause. Regarding the last, he stated:

"By the above process of exclusion it has been attempted to show that many cases of adherent pericardium are probably of tuberculous origin, although not showing any anatomical characteristics of tuberculosis. However, it is to be understood that this is not the only cause."

It was his impression that the pericarditis in many instances was secondary to tuberculosis of the mediastinal glands. Concerning the differentiation of the rheumatic and tuberculous cases, he stated:

"In the rheumatic there is a total absence of tuberculous lesions in the mediastinal glands and lungs, the pleuritis existing is generally localized at the pleuroparietal surfaces, seeming to be secondary to the pericarditis, endocardial changes are usually present, in all but one of those recorded, death is usually due to cardiac failure in the rheumatic, while this is the exception in the healed tuberculous pericarditis, the age of the subjects is, on the whole, younger in the rheumatic."

Trout in 1931 collected all cases of adhesive pericarditis in which operation had been performed. The Delorme operation had been used in 43 of these and the Brauer procedure in 54. Concerning the etiology, he stated:

"It is usually regarded that the unknown cause of rheumatism, or, in the nomenclature of today, 'arthritis from focal infection,' is the chief etiologic factor in the production of these adhesions. However, in a brief review of some of the literature, I noted that various types of streptococci, pneumococci, and staphylococci, and of tuberculosis, gonorrhea, and influenza bacilli, etc., have been reported as being intimately connected with the causation of adherent pericarditis."

Smith and Willius of the Mayo Clinic found (at necropsy) 144 cases of chronic adherent pericarditis among 373 cases of pericardial disease. Only 57 of the 144 patients had presented complaints that made the heart the major issue in the clinical picture. The etiology was determinable in 73 of the 144 cases. Rheumatic fever was the etiologic factor in 21.5 per cent, pulmonary and pleural disease in 17.4 per cent, cardiac infarction in 6.2 per cent, syphilis 2.8 per cent, neoplasms in 2.8 per cent, and tuberculosis in 2.1 per cent.

Schur in 1934 reported 17 instances of adhesive pericarditis, some of which had medi-

astinopericarditis and others constrictive pericarditis. Tuberculosis was suspected of being the etiologic agent in 5 of these, in none of which operation was performed. Seven were believed to be rheumatic in origin. The etiologic agent was not established in the first 6 patients upon whom pericardectomy was performed by Beck (4).

Rothstein in 1934 collected all instances of adhesive pericarditis in children under 15 in which the condition had been treated by operation. The total number of cases was 34. The etiologic agent was thought to be acute rheumatic fever in 16, tuberculosis in 9, and pyogenic organisms in 2. The Brauer procedure was carried out in 23 of these, which would lead one to believe that the disease was mediastinopericarditis. In the 11 remaining, pericardectomy was performed. Four of these were supposedly tuberculous in origin. Borchardt states that rheumatism is the most frequent cause of chronic adhesive pericarditis and that tuberculosis plays a relatively smaller rôle. Tuberculosis as the cause of the constrictive pericarditis was proved in only 1 of the 7 patients reported by Heuer and Stewart.

White (57) had the following to state concerning the etiology of the 15 cases of constrictive pericarditis which he and Churchill reported:

"The etiology of the chronic pericardial disease can be assigned as follows: tuberculous in two (questionable in two others), pneumonia with polyserositis (including both pleuritis and pericarditis) in two, sepsis in one, rheumatism in none, uncertain or unknown in ten (in five of which, however, there was a definite history of acute pericarditis)."

White's report is similar to our experience in that none of the patients had a rheumatic infection. He stated:

"It is of further interest that a series of 1,000 children with the rheumatic infection studied in the House of the Good Samaritan in Boston, and followed over a period of ten years has shown, in not a single instance any evidence of chronic constrictive pericarditis, even though the heart was often seriously involved in other respects and even though acute pericarditis had been noted in many cases during their acute rheumatic infection."

Of the 28 patients with constrictive pericarditis that have been observed in the Vanderbilt University Hospital in the past 11 years,

the etiological agent in 21 was established by aspiration, operation, or autopsy. The etiological agent was the tubercle bacillus in 18 and the *Staphylococcus aureus* in 3 cases. In several others, there was suggestive evidence that the tubercle bacillus was the cause of the disease. Such a preponderance of tuberculosis as a cause of constrictive pericarditis is not confirmed by most of the reports in the literature. However, these patients had pericardial fibrosis which was constricting, while many of the statements in the literature are concerned with adhesions of all types.

The most striking generalization that can be made is that a constricting scar is a frequent result of tuberculous pericarditis and a rare result, if it ever occurs, of rheumatic pericarditis. In the latter infection, there is a sticky exudate of a fibrinous character which usually in a relatively short period causes the two surfaces of the pericardium to become adherent. The acute injury is present but there is not the prolonged insult such as occurs in a tuberculous infection. The differences in the pictures of the two are shown in Figures 3 and 4. In 3 of the cases here reported constriction occurred as a sequel to infection with pyogenic organisms. It appears that this is particularly apt to occur when operation for purulent pericarditis is delayed.

#### DIAGNOSIS

The diagnosis will be discussed in part by enumerating the findings in a group of patients in the Vanderbilt Hospital. These patients have been studied carefully by Doctors C. S. Burwell, T. R. Harrison, H. J. Morgan, David Strayhorn, and others. A total of 28 patients with undoubted constrictive pericarditis have been observed in the past 11 years. The diagnosis was confirmed at the time of operation in 20 of these, in 3 there was only the clinical diagnosis, and in the 5 remaining, the pre-mortem impression was confirmed at autopsy.

The ages of the patients ranged from 14 to 77 years. The number of young patients in this series is less than that usually encountered. Only 4 of the 28 patients were females. Twenty were white and 8 were colored.

The patients have presented themselves for examination after illnesses varying from a few

days to a number of years. Most of them had been ill for a number of months rather than years. In a certain number of cases the illness has begun with a respiratory infection, but this was not always so. Most of the patients came complaining of weakness, fatigability, swelling of the abdomen, edema of the feet, and discomfort in the upper abdomen. Dyspnea on exertion was frequent; dyspnea at rest was usually a late development if it occurred at all. On examination the impressive findings were those of systemic congestion; that is, distended veins, high venous pressure, engorged liver, ascites, and peripheral edema. Pleural effusion was frequent; pulmonary edema was rare. These signs of congestion often remained essentially unchanged for weeks or even months, unlike those in most cases of heart failure. This group of signs, which point so strongly to failure of the right side of the heart, were combined with a normal sized or only slightly enlarged cardiac dullness, a fixed heart, distant heart sounds, and an absence of visible or palpable apex beat. The heart rate was rapid and the rhythm regular. Heart murmurs were absent. The blood pressure and pulse pressure were usually low. The pulse was small and diminished or disappeared during inspiration in all patients except one. Under the fluoroscope, the pulsations of the heart were found to be greatly diminished or absent. Examination of the heart by the x-ray showed areas of calcification in some patients. In this connec-

TABLE 1.—SYMPTOMS AND SIGNS IN 28 CASES OF UNDOUBTED CONSTRICTIVE PERICARDITIS

	Per cent
Distended veins.....	100
Increased venous pressure (180 to 390 mm. H <sub>2</sub> )....	100
Enlarged liver.....	100
Edema (peripheral).....	96
Tachycardia.....	100
Diminished pulsation (fluoroscope).....	100
Paradoxical pulse.....	93
Low pulse pressure.....	93
Faint heart sounds.....	96
Ascites.....	89
Pleural effusion.....	86
Greatly enlarged heart.....	0
Pulmonary edema (gross).....	0
Hypertension.....	0
Valvular disease.....	0
Systolic retractions.....	0
Auricular fibrillation.....	4
Paroxysmal dyspnea.....	4

TABLE II—CONSTRICTIVE PERICARDITIS

A Patients Cured or Greatly Improved

Patient Age—Sex	Duration of dis- ability	Ascites	Heart rate — Tem- pera- ture	Blood pressure mm hg	Para- doxical pulse	Liv- er size	Ab- sence pul- sation x ray	Venous dis- tension and pressure mm Hg	Pleu- ral effu- sion	Etiology	Peri- car- dec- tomy —De- forme	Result Remarks
1—E. Mc 25—M	5 mos	5 mos	100 98.8	110/80	+	++	+	+	R	Healed scar	Yes	Cured (Dr Bigler) 12 years since operation
2—H. C 13—M	4 mos	3 mos	110 101	106/85	++	++	+	+	R L	Staphylococ- cus aureus	Yes	Cured 8 years since operation
3—E. E 21—M	6 yrs	6 yrs	120 100	90/60	+	++	+	+	+	Healed scar	Yes	Cured 7 years since operation
4—D. D 28—M	1-3 mos	1 mo	110 102	98/84	+++	++	+	+	L R	Staphylococ- cus aureus	Yes	Cured 7 years since operation
5—J. O 15—M	2+ mos	+	110 100	100/80	++	++	+	+	L	Tuberculosis	Yes Two	Markedly improved 6 years since last operation
6—R. H. W 61—M	5 mos	3 wks	115 100	115/90	+	++	+	+	L	Tuberculosis	Yes	Well 5 years since operation
7—R. L. R 30—M	7 mos	5 mos	115 100	100/80	++	++	+	+	R L	Tuberculosis	Yes	Cured of pericarditis, 4 years since operation. Bone graft for tuberculous spine. Cured
8—W. G. A 57—M	7 mos	6 mos	105 100	124/90	+	++	+	+	R L	Tuberculosis	Yes	Markedly improved. Two years since operation
9—J. W 17—M	5 mos	3 mos	110 99	90/60	++	++	+	+	L	Tuberculosis	Yes	Well, no symptoms, 2 years since operation
10—R. G 18—F	7 mos	6 mos	110 99.6	100/82	++	++	+	+	R L	Tuberculosis	Yes	Markedly improved. Two years since operation
11—E. S. J 25—M	12 mos	5 mos	100 99.4	110/90	++	++	+	+	R L	Tuberculosis	Yes	Markedly improved 16 months since operation
12—W. B. D 24—M	3 yrs	1 yr	95 98.6	101/85	++	+	+	+	R	Healed scar	Yes	Markedly improved 20 months since operation

## B Patients Who Have Died Since Operation

13—C. W 35—M	7 mos	1 mos	110 99	118/104	++	++	+	+	R L	Tuberculosis	Yes	Died 22 hours following operation from hemorrhage (Dr Bigler)
14—J. W 51—M	4 mos	7 wks	110 101	105/90	++	++	+	+	L	Tuberculosis	Yes	Improved for 6 months. Died military tuberculosis
15—L. C 34—F	3 yrs	2+ yrs	95 90	98/74	+	++	+	+	L	Tuberculosis ?	Yes	Died 4 days following operation of pneumonia
16—B. C 40—M	6 mos	+	90 101	90/80	+	++	+	+	R	Tuberculosis	Yes	Died shortly after operation. Acute dilatation heart
17—E. C 45—M	4 mos	3 mos	100 101	108/84	+	++	+	+	L	Tuberculosis	Yes	Died 2 months after operation of military tuberculosis
18—A. H. L 40—M	7 mos	6 mos	110 101	105/85	++	++	+	+	L	Tuberculosis	Yes	Improved for 3 years. Died following reactivation of tuberculous process
19—E. B. G 52—M	8 mos	4 mos	110 100	120/110	++	++	+	+	R L	Tuberculosis	Yes	Died 3 days following operation. Myocardial necrosis. Rupture of right ventricle
20—J. B. S 14—M	6 mos	3 mos	110 100	110/95	++	++	+	+	o	Staphylococ- cus aureus	Yes	Osteomyelitis multiple, septicemia, acute and chronic pericarditis. Died 24 days after pericardectomy of bronchopneumonia

## C Clinical Diagnosis No Operation

21—T. Y 40—M	13 yrs	o	85 99	110/80	o	+	+	+	+	Tuberculosis ?	No	Operation not advised. Disability only partial
22—M. R 27—F	6 yrs	o	100 100	104/86	+	+	+	+	+	Tuberculosis ?	No	Disability only partial
23—W. B 45—M	2 yrs	3 wks	110 100	115/95	+	+	+	+	+	Tuberculosis	No	Bilateral pulmonary and renal tuberculous. Died 2 weeks after leaving hospital

TABLE II.—CONSTRICTIVE PERICARDITIS—Continued

D. Clinical and Autopsy Diagnosis  
Pericardectomy Not Performed

Patient — Age—Sex	Duration of disa- bility	Ascites	Heart rate — Tem- pera- ture	Blood pressure mms. hg.	Para- doxical pulse	Liv- er size	Ab- sence pul- sa- tion x-ray	Venous disten- tion and pressure mms. H <sub>2</sub> O	Pleu- ral ef- fu- sion	Etiology	Peri- car- dec- tomy —De- lorme	Result Remarks
24—W. K. 40—M.	2 yrs.	+	80 99	98/84	+	+	Not done ?	+	R L	Tuberculosis	No	Died one day after admission
25—J. B. 51—M.	2 mos.	+	120 103	120/100	+	+	+	+	R L	Tuberculosis	No	In hospital 5 weeks. Was believed to have effusion but had scar
26—E. N. 50—F.	4 mos.	2 mos.	150 103	101/88	+	+	+	+	R L	Tuberculosis	No	Died 13 hours after admission
27—S. N. 70—M.	5 mos.	+	110 102	94/60	+	+	+	+	R L	Tuberculosis	No	Pericardium drained 5 weeks before death (Dr. Bigger). Pericardium 1 cm. thick at autopsy
28—A. D. 77—M.	2 yrs.	+	100 100	160/90	0	+	?	+	L	Tuberculosis	No	Generalized arteriosclerosis. Slight cardiac hypertrophy and dilatation. Signs of constriction not marked

tion, it should be emphasized that calcification in the heart area may be due to factors other than disease of the pericardium. Further, calcification of the pericardium does not necessarily produce significant compression of the heart.

The electrocardiogram often showed small complexes and flat T waves. Heuer and Stewart described the following electrocardiographic changes in their patients:

"The electrocardiograms are of low voltage of QRS and T waves, and the latter may be 'cove' in form in leads I and II. The electrical axis may not shift or may shift only slightly, but too much emphasis is not to be placed upon this finding. There may be slight left or slight right axis deviation."

White (58) made the following statements regarding a comparison of the electrocardiogram in pericarditis and in coronary disease.

"The S-T interval and T wave changes resemble to a certain extent those found in coronary disease, especially those in acute occlusion, namely a low origin of the S-T interval with flattening or inversion of the Ts; there are, however, two distinct differences: (1) the T wave changes are usually consistently found downwardly directed in all three classical leads in contrast to the opposite direction of T<sub>1</sub> and T<sub>2</sub> after coronary thrombosis, and (2) the Q waves are not exaggerated in pericarditis as they are in either lead 1 or lead 3 after acute coronary occlusion. In the chest lead (Lead 4) the T waves in acute pericarditis tend to be upright instead of normally inverted."

The combination of a severe degree of peripheral congestion with a small quiet heart is the essential point in the recognition of con-

strictive pericarditis. Edema is out of proportion to the dyspnea. The peripheral signs suggest heart failure, but the heart itself supplies no basis for such failure. In a certain number of patients ascites appears before any other accumulations of fluid and leads to a diagnosis of cirrhosis or of tuberculous peritonitis. In all our cases, however, there has been evidence of obstruction to both the superior and inferior caval systems. Although the ascites is impressive, the neck veins are engorged and the venous pressure (after removal of the ascitic fluid) is usually as high in the arms as in the legs. The venous pressure remains persistently elevated and it is not altered greatly by the removal of fluid from the pleural or peritoneal cavities. A photograph of a patient of Stewart, Heuer, et al., demonstrating the venous distention, is shown in Figure 5. An analysis of the 28 cases shows that certain signs and symptoms are conspicuous by their presence and that certain others are conspicuous by their absence. These are shown in Table I. This table emphasizes the frequency with which the signs of peripheral congestion are found and the infrequency with which the signs of endocardial disease, hypertrophy, and pulmonary congestion are observed. It emphasizes the usefulness of the fluoroscopic examination and the determination of the venous pressure in the making of a diagnosis of constrictive pericarditis. Additional points of interest concerning these patients are given in Table II.

## DIFFERENTIAL DIAGNOSIS

In most cases, constrictive pericarditis can be readily recognized and the diagnosis can be made with confidence. Mistakes, however, can be made, and the following conditions, among others, should be taken into consideration in the differential diagnosis of constrictive pericarditis:

1. Other types of pericardial disease,
  - (a) fluid in the pericardium,
  - (b) mediastinopericarditis,
  - (c) polyserositis.
2. Diseases of the heart,
  - (a) tricuspid valve disease,
  - (b) diseases accompanied by failure of the right ventricle: mitral stenosis, cor pulmonale, myocardial disease (especially that due to coronary insufficiency).
3. Extracardiac disease,
  - (a) cirrhosis of the liver,
  - (b) mediastinal tumors,
  - (c) nutritional edema,
  - (d) multiple thrombosis of veins
  - (e) conditions associated with marked increase in intrathoracic pressure.

1. *Other types of pericardial disease.* (a) Fluid in the pericardium may bring about cardiac tamponade with symptoms and signs (depending on rapidity of accumulation of fluid) similar to those of obstruction from pericardial constriction. If this is so, the fluid usually leads to changes in the size and shape of the heart-pericardium outline which are quite different from those seen in constrictive disease. When, during the course of subacute pericarditis, the heart-pericardium shadow becomes smaller and the signs of tamponade persist, the suggestion of the formation of a constricting scar is strong. Noth and Barnes observed differences in the electrocardiographic curve in acute and chronic pericarditis. In the acute form, there is often elevation of the RS-T segment and there may be exaggerated T-waves in the standard leads. In constrictive pericarditis, the T-waves are usually flat or inverted and the QRS complexes small.

b. Mediastinopericarditis is discussed elsewhere in this paper and will be mentioned only briefly in this discussion of the diagnosis of constrictive pericarditis. It is important to make a correct diagnosis between these two types of pericardial disease, since their treat-

ment is quite different, and since the treatment of the constrictive form may be highly successful. It is suggested, especially in older literature, that these two forms of fibrous pericarditis are often associated, but this is not the experience of most observers in America. Mediastinopericarditis is usually a sequel of rheumatic pericarditis and is almost always associated with valvular disease (often multiple) and with marked cardiac enlargement. Both valve disease and cardiac enlargement are rare in patients with constrictive pericarditis. Finally, since in mediastinopericarditis, the heart is firmly bound by fibrous tissue to neighboring organs, there are signs which indicate the tugging of the heart on these adjacent structures. These signs, such as systolic retraction of the ribs and diaphragm, are not observed in characteristic examples of constrictive pericarditis.

c. Polyserositis, or the simultaneous inflammation of several serous cavities, is usually due to tuberculosis. It begins as an acute process with varying quantities of fluid and may progress to a chronic fibrous state. If the latter stage is reached, it may be difficult or impossible to differentiate it from chronic constrictive pericarditis due to other causes. In fact, we know that true constriction and polyserositis may occur at the same time. White (57) states, "Perihepatitis, perisplenitis, and even frosting of the intestine itself may occur quite independently of pericarditis or pleuritis, they may be found associated or as isolated lesions." The points of most significance in assessing the relative importance of inflammation and obstruction are the type of fluid (evidence of inflammatory origin) and the venous pressure.

2. *Diseases of the heart* (a) Tricuspid valve disease brings about circulatory changes similar to those caused by constrictive pericarditis and therefore may be associated with similar signs. Both lesions offer an obstacle to the entry of blood into the heart, in one case an obstructive valve lesion in the other interference with ventricular dilatation. Tricuspid disease is usually accompanied by other valve disease, by enlargement of the right auricle, and by veins which exhibit pulsation with ventricular systole.

b. Conditions accompanied by preponderant failure of the right ventricle include mitral stenosis, cor pulmonale, and occasionally myocardial disease. Right ventricular failure produces peripheral congestion similar to that of constrictive disease except that the congestion of muscular failure is more apt to fluctuate in severity than is that of mechanical obstruction. In addition, such cases of failure rarely exhibit pulsus paradoxus, and they usually show cardiac enlargement and other evidences of heart disease. A patient with cor pulmonale due to pulmonary vascular disease may show cyanosis, local signs of pulmonary disease, and a large right ventricle.

Myocardial disease may produce special difficulties, as exemplified by the following case:

H. M., white male, aged 44 years, entered the Vanderbilt Hospital on May 15, 1935, complaining of "abscess in chest." He was stabbed in the posterior part of his right chest 2 months previously with a long large knife. There was profuse bleeding from a sucking wound. The opening was closed and he remained in bed for a week. However, daily temperature elevations increased and he became dyspneic 3 weeks following the injury. Shortly following this, the old wound opened spontaneously and pus drained for a week. The shortness of breath was less marked following the drainage. In a few days, the wound again healed and subsequently opened spontaneously. The patient had lost 30 pounds during his illness. The past history was negative.

On examination, it was found that the patient had a chronic empyema on the right. In the right scapular line, there was a recent wound extending from the eighth to tenth interspaces with a small sinus near its center. There was a small amount of drainage from it. X-ray examination revealed hydro-pneumothorax on the right with marked fibrosis on the left. The empyema cavity was given adequate drainage by rib resection on May 17. He insisted upon leaving the hospital several weeks later, at which time the cavity held 100 cubic centimeters.

The patient re-entered the hospital on September 27, 14 weeks following his discharge. One week after having left the hospital, his physician injected some paste into the cavity. The opening closed shortly thereafter. The patient became short of breath 3 weeks prior to his return to the hospital and fullness of the abdomen and edema were noted. On examination, the patient was found at this time to be short of breath and cyanotic. The superficial veins were quite prominent, the pressure being 238 millimeters of water by a method rarely registering over 120 millimeters in a normal person. There was edema of the lower extremities and the sacral region. The pulse volume was small and distinctly paradoxical in character. The arterial blood pressure was 98/80.

The heart was somewhat enlarged and showed very little pulsation under the fluoroscope. The sounds were distant and no murmurs were heard. The liver edge extended well below the costal margin. The impression of Dr. Hugh Morgan was as follows: "Pleuromediastinopericarditis. It seems probable that the obstruction to inflow of blood to heart is about the cavae and that we are not dealing with a generalized constrictive pericarditis."

An exploration of the pericardium was decided upon and this was carried out 4 days following his admission. The pericardium looked essentially normal and no abnormality was encountered except for the escape of a small amount of blood tinged fluid upon opening the cavity. There were no adhesions between the heart and pericardium. Incision was closed without drainage. Wound healed and patient's condition remained the same for 10 days when he became suddenly worse and died 2 days later.

An autopsy was obtained, and the following observations were made. The left pleural cavity contained 600 cubic centimeters of fluid and the peritoneal cavity 2,000 cubic centimeters. A pasty mass was found in the right pleural cavity. The pericardium was essentially normal. The superior and inferior vena cavae appeared normal. The heart weighed 550 grams, and the musculature was pale in color and flabby in consistency. There was a large mural thrombus on the posterior wall of the right auricle and also one about 3 centimeters in diameter on the posterior lateral surface of the left ventricle. On cut section the musculature at the apex of the right ventricle showed several small depressed areas about one-fourth centimeter in diameter which were of a dull red color. They were also present in the left ventricular wall. Microscopic study showed thickening of the endocardium and many phases of degeneration and necrosis of the myocardial fibers. There were large areas of fresh hemorrhage scattered throughout the myocardium and in these areas, necrosis of the muscle cells was pronounced. The muscle fibers were everywhere hypertrophied and the nuclei were large and vesicular. In most areas, however, they were fragmented and stained irregularly. The liver presented a uniform picture of acute necrosis of all the parenchymal cells surrounding the central veins. The impression from autopsy was that the patient died of cardiac dilatation and hypertrophy, myocarditis and endocarditis. This case is cited to show that some of the signs seen with constrictive pericarditis may be present in other conditions and to emphasize that it is not any single sign but a total picture that is distinctive.

A combination of right ventricular failure with a small amount of pericardial fluid led in another case to an incorrect diagnosis of constrictive pericarditis.

E. A., a white female, aged 35 years, entered the hospital on December 8, 1934, complaining of "swelling of abdomen."



Nine months previously, the patient noticed that her abdomen was increasing in size, and edema of the feet and face appeared. This was followed by shortness of breath. She became extremely weak and complained of palpitation and dizziness. She was treated with diuretic drugs and digitalis and some improvement followed, but the dyspnea and edema never disappeared entirely. There had been frequent attacks of epistaxis during the 2 months preceding her admission, and nausea had been present for a week. There had been a gain in weight of 13 pounds during the illness.

The face was swollen and the superficial veins of the entire body were unusually prominent. The retinal veins were distended. The pressure in veins of the arms and legs was 172 millimeters water. There was evidence of a slight increase in the size of the heart-pericardium by both physical examination and x-ray. The pulsations of the heart were indistinct under the fluoroscope. The blood pressure was 118/104 millimeters mercury and the pulse was believed not to be paradoxical. There was a good deal of fluid in the left pleural cavity. The liver extended seven fingers breadth below the right costal margin in the midclavicular line and there was evidence of free fluid in the peritoneal cavity. The temperature was 101 degrees F. and the pulse 100. The electrocardiographic tracing showed (1) notched QRS in all leads, and (2) no shift in axis. The cerebrospinal fluid pressure was 210 millimeters water.

She developed a generalized macular rash which was associated with a cough and an increase in temperature, and she died 23 days following her admission to the hospital. An autopsy was obtained. The peritoneal cavity contained one liter of straw colored fluid and each pleural cavity approximately 1,200 cubic centimeters. There was a small pericardial effusion (340 c.cm.) and there was an extensive and obviously important degeneration of the right ventricular muscle on the basis of vascular disease. This involvement of the right ventricle appeared to account for the congestive phenomena. The pericardial effusion probably accounted for the reduced pulsation. The combination of pure ventricular failure with a small amount of pericardial fluid was mistaken by us for constrictive pericarditis.

3. *Extracardiac disease.* (a) Portal cirrhosis. There should be little difficulty in differentiating constrictive pericarditis from portal cirrhosis of the liver. The possibility of confusion is illustrated by the fact that a number of patients with constrictive pericarditis have had an omentopexy, usually without benefit. The absence of a history suggestive of cirrhosis of the liver, the presence of a paradoxical pulse, the elevated pressure in the neck and arm veins, and the decreased pulsations of the heart should serve to make the diagnosis of chronic constrictive pericarditis. It is well to

remember that both diseases may be present.

An example of chronic constrictive pericarditis, which had been diagnosed erroneously as cirrhosis of the liver, is presented in detail. An omentopexy had been performed in an effort to improve his condition.

E. E., a white male farmer of 21 years, entered the Vanderbilt University Hospital on August 17, 1934, complaining of swelling of the abdomen and shortness of breath.

On December 28, 1929, 5 years before admission, this patient began to ache throughout his body. His physician said that he had either influenza or pneumonia. He went to bed and remained there 3 days before returning to work. Approximately 2 weeks after returning to work, the patient began to be short of breath. A diagnosis of empyema was made: a resection of two ribs on the left side was performed, and pus was encountered in the pleural cavity. He was in the hospital for 9 days and upon getting out felt quite well for 2 or 3 weeks. Shortly thereafter he noticed swelling in sundry parts of his body in the following order: scrotum, legs and thighs, abdomen, arms, face and eyes. The swelling of the face was quite marked in the morning but disappeared during the day. Coincident with the generalized edema he became more short of breath. He did not feel strong enough to return to work. In April, 1930, he was given diuretics which reduced the amount of edema, and he felt much better for about 5 months when his abdomen began to enlarge again. In the summer of 1931, he went to a hospital where he remained for 47 days. Three abdominal paracenteses were performed and 13, 8, and 9 liters of fluid were removed from his abdomen. An omentopexy was performed during this stay in the hospital. Following his discharge, he got along fairly well until the winter of 1933 when he began having mild chills with fever at intervals. Several times he coughed up small amounts of blood. In March, 1934, while loading hay, he was struck on the left side of the abdomen by a hay fork which he was using. After this blow his abdomen was tender to pressure, and began to increase gradually in size. On April 26, 1934, he again entered another hospital for a period of 19 days. Fluid was withdrawn from his right chest at that time. Following this, it was necessary for him to return to the hospital on several occasions and on each visit fluid was withdrawn from the chest. The patient had been at home for 6 weeks previous to his admission to the Vanderbilt University Hospital.

On examination he was found to be a poorly nourished white male who did not appear acutely ill. He was slightly dyspneic while lying flat in bed. There was marked engorgement of the neck veins when he was lying flat in bed, but this prominence of the veins disappeared when he sat up. There was marked fullness of the lower half of chest, with definite increase in the anteroposterior diameter. Expansion was

limited on both sides, and this limitation was most marked on the right. There was dullness (in some areas flatness) over the entire right chest, with markedly diminished breath sounds. The left chest was resonant throughout except for dullness in the lower half of the back. There were diminished breath sounds in this area. The heart sounds were distant; there were no murmurs. There was no shifting of the cardiac dullness with change in position. The veins of the chest wall were unusually prominent.

The abdomen was distended. There was a definite fluid wave and shifting dullness was present. The liver was felt 6 centimeters below the right costal margin. The edge of the liver was firm and smooth. There was a hernia at the lower part of an abdominal scar.

The temperature was 99 degrees F., the pulse rate 120 per minute, respirations 21, and the arterial blood pressure was 90/60 millimeters mercury.

The x-ray report at the time of this admission was as follows: "There has been a resection of the left ninth rib posteriorly. Slight thickening of the pleura in the left costophrenic angle. Practically complete obliteration of the right lung field due to fluid and thickened pleura. The right border of the heart is not made out. Practically no pulsations seen in the cardiac shadow on the left side. No activity seen in the left lung."

Electrocardiographic study revealed notched QRS in all leads and no shift of axis.

The patient was discharged from the hospital September 2, 1934, and readmitted September 24, 1934. During this time his condition had remained practically the same. The venous pressure at the time of second admission was 195 millimeters water. The circulation time, arm to carotid, was 52 seconds by the sodium cyanide method. After further observation it was decided that this patient should have a decortication of the heart.

Operation was performed October 4, 1934. A left parasternal incision was made and the third, fourth, and fifth costal cartilages, together with parts of the ribs, were removed. There were many dilated veins beneath the cartilages. No cardiac pulsations were visible when the pericardium was exposed. Incision was made through a thickened scar which was 7 to 10 millimeters in thickness. Good pulsation of the heart was noted after a part of the scar had been removed. An area of scar approximately 6 by 6 centimeters was cut away. A great deal more of the scar which was not removed was freed from the heart. Good pulsations resulted. The wound was closed without drainage. Microscopic sections showed a thickened, fibrous membrane which was quite vascular on its outer surface.

Following the operation, the patient made a slow but progressive improvement. He returned to the hospital approximately 1 year following the pericardectomy for repair of the hernia at the site of the omentopexy. He has been performing hard manual labor for the past 5 years. Normal pulsations of the heart are visible under the fluoroscope.

b. Mediastinal tumors. A tumor which is located in such position that it compresses the superior and inferior vena cavae may be associated with findings which are quite similar to those caused by constrictive pericarditis. There is less apt to be a general suppression of the pulsations of the heart in the patient with a mediastinal tumor, and more apt to be a greater venous pressure in one caval area than in the other.

c. Nutritional edema. The differentiation between edema due to constrictive pericarditis and nutritional, which it may simulate, depends primarily on the determination of the venous pressure and the concentration of serum proteins. The former is elevated in constrictive pericarditis and normal in uncomplicated nutritional and nephrotic edema. The serum proteins (and colloid osmotic pressure) are lowered in nephrosis and nutritional edema and normal or only slightly lowered in constrictive pericarditis. Nutritional edema, however, occurs as a complication of many other diseases, including chronic heart disease, and hence may add to the edema of constrictive pericarditis, the lowered serum proteins augmenting the edema-producing effect of the increased venous pressure. Under these conditions the relative importance of the nutritional factor may be judged from the level of the serum proteins or the colloid osmotic pressure.

d. Multiple thrombosis of veins. A patient with multiple thrombosis of veins has been observed who presented a picture highly suggestive of chronic constrictive pericarditis except that the pressure in the tributaries of the superior vena cava was slightly lower than that usually found in the latter condition. A description of this case follows.

O. A. A., colored, aged 19 years, entered the Vanderbilt University Hospital January 2, 1936, with a complaint of "swollen sore stomach and headaches." Slight weakness and shortness of breath was observed 2 years previously. Seven months prior to admission, he noted enlargement of the abdomen and a mass was felt extending below the costal margin. The mass was somewhat tender to pressure. In addition, he had had some pain of both the right and left sides of the chest. The findings on examination included prominent veins of the abdomen and chest, a greatly enlarged liver and spleen, and dullness in the flanks. The arterial blood pressure was 155/130. The venous pressure in an arm vein was 125 milli-

meters water. The red blood cell count was 7,000,000 and the hemoglobin 16 grams. Fluoroscopic examination of the heart showed definite but small pulsations.

An exploratory laparotomy was performed, and the veins of the omentum were found to be tremendously enlarged and distended. The liver was greatly enlarged and quite dark in color. The spleen was enlarged and hard. There was a moderate amount of free peritoneal fluid. The impression was that there was partial obstruction of the hepatic veins. The patient died subsequently and an autopsy was performed. There was a definite constriction of the inferior vena cava as it passed through the groove in the liver. At this point the circumference of the vena cava was only 2.5 centimeters whereas its circumference was 7.5 centimeters at the level of the entrance of the renal veins. The constricted area was 8 centimeters long. The wall of the vein was thickened, apparently due to fibrous tissue. The hepatic vein orifices were smaller than normal and several contained thrombi. In addition, there was thrombosis of the splenic vein. The pericardium and heart were normal. A photograph of the veins is shown in Figure 6.

e. Conditions associated with a marked increase in the intrathoracic pressure may be confusing and occasionally there may be difficulty in differentiating diseases such as chronic asthma from constrictive pericarditis. In these conditions the heart is usually small and the venous pressure is elevated. A paradoxical pulse may be present. Differentiation may be made on the basis of signs of pulmonary disease.

#### INDICATIONS FOR AND TIME OF OPERATION

It is generally agreed that an acute pyogenic pericarditis should be drained and that an acute tuberculous pericarditis with a large accumulation of fluid should be treated by aspiration rather than by open drainage. It is accepted that when constriction is associated with a pyogenic infection, an appropriate amount of thickened pericardium should be removed, and the infected area should be drained. It is generally agreed that a pericardectomy should be performed when a patient has constrictive pericarditis of marked degree due to a process, tuberculous or otherwise in origin, which is healed or inactive. If the disability is only partial and is not progressing, operation may be postponed with the hope that it will not be necessary. If one is convinced that an operation will be necessary,

there is danger in postponing it after the chronic stage of the disease has been reached. Delay results in greater atrophy of the myocardium and the dangers of entering the heart cavities during the decortication and of dilatation of the heart at and subsequent to the operation are increased. In other words, pericardectomy is indicated when the active process has been replaced by a healed scar and before marked cardiac muscular atrophy occurs.

It is obvious that the patient does not always present himself at this ideal time. There is a variation in the time required for an active tuberculous infection to become healed. It may be stated in general that an interval of at least 6 months and preferably a longer time should separate the initial infection and the removal of the scar. As will be pointed out subsequently, however, the unfavorable course of the patient may render imperative an earlier operation.

There is a difference of opinion as to the attitude which should be adopted when the constriction is caused by a thickened pericardium and epicardium in which a tuberculous infection is still present and when the patient's condition is becoming progressively worse. A frequent occurrence in tuberculous pericarditis is the development of increased signs of systemic congestion as the fluid disappears from the pericardium and as the heart-pericardium shadow becomes smaller. The patient who has constriction and an active tuberculous infection has both as causes for his signs and symptoms, and the treatment is unusually complicated. Most of the patients, studied and operated upon by us, have had activity in the sense of demonstrable tubercles in the pericardium and epicardium but have not had proliferative activity with fluid. The stage of the disease that has been present in most of our patients at the time of operation is demonstrated in Figure 7 and the more active proliferative stage in which operation should be avoided, if possible, is shown in Figure 8.

Volhard expressed the opinion that the proliferative stage of tuberculous pericarditis is not well suited for operation. Churchill (24) stated:

"Active tuberculosis of the pericardium may produce the entire syndrome of chronic constrictive pericarditis. The point at issue is whether operation can be effective if performed during the active phase of the infection. The reports in the literature of operations performed during this period are uniformly discouraging and confirm our personal experience."

The authors agree entirely that the operative procedure is easier and that the mortality rate is lower if operation can be postponed until the tuberculous process has become inactive. Such has not always been possible in our experience because of the unfavorable course of the disease. The general policy which has been adopted is that the operation should be deferred during the active stage as long as the patient's condition is stationary or is improving. If, however, the patient is losing ground and the venous pressure is rising despite the fact that the heart-pericardium shadow is decreasing, indicating the disappearance of fluid, operation should be proceeded with even though some activity is still present. Even in the presence of proliferative activity without fluid, operation may be practicable and the decision for or against it should be made on the basis of the severity of the interference with the circulation rather than on the basis of the presence or absence of activity of the tuberculous process. One has to evaluate the relative rôles of constriction and of infection. If constriction is responsible for most of the symptoms and signs, operation is indicated; if infection is responsible for the predominating features of the illness, nonoperative treatment is to be preferred. If both infection and obstruction are important in producing the disability, one should attempt to make the difficult decision as to therapy after balancing the advantages and disadvantages of operative and nonoperative treatment.

This discussion would be incomplete without a consideration of the treatment of patients in whom the obstruction is only moderately severe. Since a moderate amount of danger in association with pericardectomy is inescapable, nonoperative treatment is usually advisable if the disease is not progressive and if the disability is not severe. Under these circumstances, measures such as the restriction of fluid and salt intake, the use of diur-

etics and the aspiration of serous cavities, if indicated, will usually add to the comfort and reduce the incapacity of patients. Digitalis is not effective save in the rare cases in which there is heart failure as well as obstruction.

In summary, one should realize in considering the indications for and the time of operation that successful therapy is dependent upon the ability of the surgeon to remove enough scar to release the heart, upon the capacity of the weakened heart muscle to perform its work, and upon the nonprogression of the inciting disease. The decision as to therapy is in many instances a difficult one to make.

#### THE OPERATION

*Preoperative treatment.* After it has been decided that pericardectomy is indicated, the patient should be got into the best possible condition. This consists in the main of reducing to a minimum the results of the pericardial constriction, that is, the edema, ascites, and pleural effusion. This part of the treatment is similar in most respects to that of heart failure. The patients should be placed on a low salt diet (approximately 2.0 grams daily) and the fluid intake should be limited to approximately 1,500 cubic centimeters daily. If the blood studies show a reduction of plasma proteins, which is a frequent finding, a high protein diet should be given. Large accumulations of fluid in the pleural or peritoneal cavities should be removed by aspiration. Any one of a number of diuretics may be used in an attempt to cause the disappearance of edema. There is a variation in the individual response to these agents. The advice of Heuer and Stewart is as follows:

"Of the drugs used to mobilize fluids, mercurpurin has been found to be the most satisfactory. It is usually given in 2.0 cubic centimeter doses intravenously at 3 day intervals. To some patients ammonium chloride, 3 grams per day, was given at the same time to enhance the diuretic effect. Theocalcin, 4.5 grams daily, urea, 30 cubic centimeters of a 50 per cent solution, twice daily and aminophyllin 0.1 gram 3 times per day were all tried but with less effect."

Regardless of the agent used, the patient should be rendered free of as much excess fluid as possible. It is particularly important that large accumulations of fluid in the pleural

cavities should be removed prior to the anesthetic and operation.

An interesting question is concerned with whether or not patients with constrictive pericarditis should be digitalized, and particularly so when operation is contemplated. Harrison and Leonard have shown that digitalis decreases the output of the heart of normal dogs. Burwell, Neighbors, and Regen (20) found that it decreases the cardiac output in normal men. Burwell and Strayhorn (21) found in a patient with constrictive pericarditis that digitalis decreased the cardiac output per minute due chiefly to a decrease in rate with little change in the output per beat. Harvey and Whitehill state:

"Inasmuch as these patients seem abnormally sensitive to digitalis and develop cardiac arrhythmias with small doses, and since the heart failure is usually due to cardiac tamponade, the drug, generally, is not indicated. In those patients who continue in failure after the pericardial fluid has been removed, particularly the older ones with arteriosclerosis, it might be useful."

Burwell (16) states that there are 3 important exceptions to the general rule of the nonusefulness of digitalis in these patients: the occasional patient who has auricular fibrillation with tachycardia in addition to pericardial obstruction; the patient about to be subjected to pericardectomy whose possibly atrophied myocardium may have imposed upon it increased demands if the operation relieves the obstruction to inflow, and the patient who has both obstruction and myocardial insufficiency.

Preanesthetic sedatives should be given in moderate amounts but not to the extent that the respirations are depressed. Compatible blood should be available for transfusion in case such is found to be necessary as a result of copious bleeding during the operation. Fluids, including blood, should not be introduced intravenously unless absolutely necessary.

**The anesthetic.** There is no unanimity of opinion as to the most desirable anesthetic agent for this operation. Most surgeons are agreed that general anesthesia is indicated because of the magnitude of the procedure and of the possibility of the accidental injury of the heart muscle and of opening one or both pleural cavities. It is because of the latter

possibility that Churchill (24) uses intratracheal anesthesia, the gas-oxygen-ether sequence being employed. Of the 7 patients subjected to pericardectomy by Heuer, 4 were anesthetized by the open drop ether method, 2 with drop ether administered through an intratracheal tube (Magill), and ethylene-oxygen-ether mixture was used in the remaining patient. Harrington used cyclopropane as the anesthetic agent in the 9 patients on whom pericardectomy was performed. This was administered through a tightly fitting mask but he cautions that an intratracheal tube should be available for use if necessary. In the author's experience, the agents which have been used include local alone, local combined with nitrous oxide and oxygen, with cyclopropane and oxygen and with gas-oxygen-ether. Our routine at present consists of local infiltration for the incision and removal of bony structures followed by the gas-oxygen-ether sequence during the time that the pericardial scar is being removed. Usually an intratracheal tube is not employed. The most unsuitable agent that we have used is nitrous oxide. It is impossible to obtain satisfactory anesthesia without causing anoxia. There is a pre existing impairment of the circulation of the heart muscle as well as structures elsewhere and it is unwise to cause additional anoxia.

The impression exists, without definite proof, that cyclopropane may exert toxic effects on the heart. Robbins and Baxter (44) found that the cardiac irregularities which develop at the time of, or soon after, respiratory arrest as caused by cyclopropane are not due to the anesthetic agent itself but to anoxemia. They noted further (45) that cardiac irregularities which are observed in dogs under cyclopropane anesthesia after premedication with morphine may be abolished by barbital or amytal. In view of these findings, it appears that a barbiturate rather than morphine should be employed when cyclopropane is to be used. As stated previously, it is our impression that gas-oxygen-ether is preferable to oxygen-cyclopropane in operations on the heart.

Beck and his associates (3, 6) found in animals that exposure of the heart and great vessels to atmospheric air pressure results in a significant reduction in the cardiac output.

As a result of these observations, they recommended the revival of the use of the Sauerbruch negative pressure chamber. One of us (A. B.) was unable to confirm the experimental observations under slightly modified conditions (10). At any rate, a diametrically opposite viewpoint to that of Beck is expressed by Churchill (24). He states:

"While Beck focuses his attention upon failure of the peripheral circulation from a reduced filling of the heart, I consider the real hazard of the operation to lie in exposing the weakened musculature of the heart after it has been released from the scar to too great a venous return. From this point of view the effect of atmospheric pressure on the surface of the heart would be welcomed. I have deliberately attempted to reduce the venous return to the heart during and immediately following the operation."

Measures which may be used to reduce the venous return, include the upright position and the reduction of the blood volume by bleeding. However, as Churchill has emphasized, it must be remembered that a reduction in the effective venous pressure may be dangerous if the heart is not relieved of its constricting scar.

*Position of patient.* The patient should be placed on the operating table on his back in either the recumbent or semirecumbent position. Churchill (24) and Schmieden (48) prefer a slightly upright position, using a dental chair, in order to reduce somewhat the venous return to the heart. There is no strong objection to the recumbent position unless the patient is dyspneic.

*Exposure of pericardium.* Most surgeons are agreed that the operation should be performed through an extrapleural approach and that the incision should be made to the left of the sternum. Median sternotomy is not necessary as an adequate exposure can be obtained through a left parasternal incision. The incision should be such that the heart can be exposed from base to apex. The midportion of the incision should be over the sternum or at its left border and the lateral projections of the incision should overlie the uppermost and lowermost costal cartilages which are to be resected, extending to the midclavicular line. The pectoralis major muscle is freed from the sternal border and is reflected laterally with the skin flap. It is usually advisable to remove

the third, fourth, fifth, and sixth costal cartilages and short segments of the adjoining ribs. There is a difference of opinion as to whether the perichondrium and periosteum should be included with the cartilages and ribs. Both Heuer and Harrington state that it is not necessary to include them. The present authors agree with Schmieden (48) and with Churchill (24) that it is desirable to have a flexible precordial area over the liberated heart and that the perichondrium should be removed in order to avoid regeneration. Furthermore, it is our impression that one is less apt to have a chronic discharging sinus when the process is tuberculous in origin if perichondrium is removed. In this connection, it is quite important that all cartilage which is damaged should be removed. The intercostal muscles are divided at the left sternal border, and the internal mammary artery and vein are usually ligated at the upper and lower extremes of the incision. The thin layer of muscle and connective tissue overlying the pericardium is divided, and the left half of the sternum is removed with rongeurs or the Lebsche sternum knife.

Beginning at the left sternal border near the lower end of the incision, the left pleura is dissected laterally for a considerable distance, preferably to the left phrenic nerve. It is well to remember that there may be no so-called "area of safety" and that the right and left pleural reflections may be in contact with each other. In most instances, the greater part of the dissection of the pleura may be carried out by blunt dissection, a thin layer of gauze applied to a finger being used. The experience of most surgeons is that an opening is made in the pleura during the dissection in about one third of the operations. This usually causes no embarrassment to the respirations and it is unnecessary in most instances to attempt closure of the tear in the pleura. As will be commented upon subsequently, an additional reason for not closing a pleural opening is that there are some points in favor of drainage of the decorticated area into the pleural cavity unless pyogenic organisms are present. It is our policy to delay dissection of the right pleural reflection until after removal of the pericardial scar has been begun.

In the sickest patients, particularly the elderly, Bigger (36) has suggested that the operation should be performed in stages. At the first stage, the rigid structures of the chest wall may be resected and a small portion of the scar near the left border of the heart may be removed. At the second stage, the further removal of scar may be carried out through the same incision or through a corresponding incision to the right of the sternum.

*Removal of scar.* Before the technical features concerned with the removal of the scar are considered, points of importance in connection with the choice of site for the beginning of the decortication and also the extent of the decortication will be considered. It should be borne in mind in this discussion that it is impossible before beginning the removal of scar to distinguish the various parts of the heart. The left ventricle lies almost entirely laterally and posteriorly, and the portion of the heart in contact with the anterior chest wall is largely the right ventricle. The most frequent mistake is the assumption that one is decorticating the left ventricle when in reality it is the right one. First, the site for the initial removal of the scar will be discussed. It is generally believed that it is important to liberate part of the left ventricle from the scar before decorticating the right ventricle. The reasons for this are two in number. The muscle of the left ventricle is thicker than that of the right, and there is less danger on the left of entering the cavity of the heart when one is attempting to establish a line of cleavage between the heart muscle and the scar. The second reason for freeing the left ventricle first is the theoretical danger of pulmonary edema. Initial release of the right ventricle permits a greater flow of blood into it and thence into the lungs. Since the transmission of blood through the lungs has not been facilitated by decortication of the left ventricle there may result an increase in the amount of blood in the lungs. This in time may lead either to pulmonary edema or to dilatation and failure of the right ventricle. This reasoning appears to be sound but in actual practice we have seen no harmful effects in those instances in which the right ventricle has been decorticated before the

left. As stated previously, it is our impression that the surface of the right ventricle is often believed to be that of the left one.

The second point has to do with the extent to which the decortication should be performed. There is some difference of opinion on this subject. Most are agreed that actual decortication of the auricles is a hazardous procedure due to their thin walls and should not be attempted. If the ventricles are properly freed of scar, the undecorticated auricles are able to conduct sufficient blood to the ventricles to supply the needs of the body. Churchill (24) states that free motion of the right auriculoventricular groove is an important physiological mechanism in the action of the right heart and that every effort should be made to free this area of scar. Several observers have commented on the need for the removal of the scar from the site at which the vena cavae enter the heart. It is our impression that this is rarely necessary and even more rarely accomplished successfully. The extent of the removal of scar as advocated by Heuer is as follows:

"We have removed as completely as possible the pericardium over the left and right ventricles, but have not attempted to remove the adherent pericardium over the auricles. An effort has been made to free the apex, and if possible the dissection is carried well down on the diaphragmatic portion of the pericardium. No attempt has been made to go beyond the right auriculoventricular groove, nor have we attempted to free the great vessels at the base."

Schmieden (48) states that complete liberation of the left ventricle is the most important part of the procedure and that in most cases this is the only surgical measure that is necessary. We question seriously the correction of this view. Most patients with constrictive pericarditis have remarkably little dyspnea and edema of the lungs in comparison with the marked evidence of congestion in the systemic circulation. Most of the signs and symptoms are attributable to back pressure from the right side of the heart. In our experience, major emphasis has been devoted to decorticating the right ventricle. In one patient who has obtained a good result, all or certainly most of the decortication was performed on the right, since bleeding from an unknown source had been encountered during



Fig. 9. Section showing an active tuberculous infection of scar. Note the large artery which is intimately attached to the scar. Autopsy specimen.  $\times 20$ .



Fig. 10. Section showing caseation and giant cells. Note the large blood vessel which is anchored more firmly to the scar than to the heart muscle. Autopsy specimen.  $\times 16$ .

the attempt to remove scar from the left ventricle.

We shall return now to a description of the operative procedure itself. After having obtained an exposure of the pericardium which extends to or almost to the left phrenic nerve, an incision is made into the scar overlying the left ventricle. This is probably the most tedious part of the operation. Much of the ease and success of the operation is dependent upon finding the correct plane of cleavage. It should be remembered that it does little if any good to remove the scarred pericardium if thickened fibrous epicardium is left behind. The plane of cleavage should lie preferably between the layer of organized exudate on the exterior of the epicardium and the epicardium itself. It should not lie immediately next to or in the heart muscle. As is well known, the major coronary arteries are located quite superficially. If one is unable to establish the correct plane of cleavage, the point of attack should be shifted. Usually slight motion of the heart can be seen when the incision in the scar has been extended to the correct depth. The incised edges of the scar are then grasped with instruments, and the decortication is extended by sharp and blunt dissection. A sharp instrument should be used for the division of all strands of scar tissue which extend into the heart muscle. One may encounter areas in which there are unusually dense adhesions

and the cleavage plane is lost. As Churchill (24) has stated, this is particularly apt to be encountered in the region of the left descending coronary artery. This area should be approached with caution in order to avoid injury to this important vessel. If one is unable to be certain as to the relationship of the scar to the vessel, dissection at that point should be abandoned temporarily and a cleavage plane further to the right should be found.

As the sternum is approached, it is usually easy to push the right pleural reflection laterally with gauze if the heart is dislocated slightly to the left by making traction on the scar. One should pause frequently during the dissection of the scar in order to allow the heart to regain its normal rhythm. Bigger (8) has pointed out the importance of not excising the scar as it is freed and of leaving temporarily a flap of the tissue at the point of the dissection in order that it may be used for covering a rent in the heart muscle if this unfortunate accident occurs. As has been stated, the removal of the scar should be extended, if it is feasible, to the region of the phrenic nerve on the left, to the neighborhood of the inferior vena cava on the right, and the apex of the heart should be liberated. The scar that is removed usually measures approximately 8 by 10 centimeters, and it may vary in thickness from 1 millimeter to more than 1 centimeter. It is very gratifying to note that the



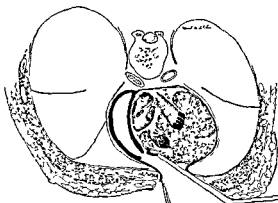


Fig. 11. Method for developing a new line of cleavage to separate the inner wall of cavity containing fluid from the surface of the heart. (From Churchill, I. D., *Ann. Surg.*, 1936, 104: 522.)

removal of a relatively small area of scar tissue will result in the freeing of a rather large part of the surface of the heart.

There are several points which deserve additional comment. As has been stated, calcification of the pericardium may or may not be present. If present, there may be a complete bony shell. The calcified tissue may extend into the heart muscle, and in such instances one is particularly likely to make an opening into a cavity of the heart. One should not hesitate to leave isolated areas of fibrous tissue or calcium if the danger of damaging the heart wall in the dissection appears to be great.

As has been stated, the large coronary vessels have a superficial position and are apt to be injured in the process of removing the scar. Sections of several autopsy specimens show that these vessels may become more intimately attached to the scar tissue than to the underlying heart muscle. Examples of this are shown in Figures 9 and 10. The death of one of our patients probably resulted from including a large branch of a coronary artery with the scar that was removed. Autopsy revealed rupture of the heart at the site of necrosis of part of the wall of the right ventricle. As has been pointed out, Churchill (24) recommends extreme caution when approaching the sulcus formed by the left descending coronary artery. This may be approached from both sides after a plane of cleavage to the right and left of it has been established.

In an occasional case in which the major part of the pericardial cavity is obliterated, one may find an encapsulated area of fluid, both the pericardium and epicardium being thickened. Churchill (24) has emphasized the importance of removing the wall of the cavity that is in contact with the surface of the heart. Little good results simply from removing the wall that corresponds with the parietal pericardium. The point at which the line of cleavage should be developed is shown in Figure 11 (from Churchill).

If the right ventricle cannot be decorticated properly at the primary operation through the left parasternal incision, this can be attempted subsequently through a similar incision on the right. This has not been necessary in our experience. If the apex of heart cannot be liberated, Schmieden (48) states that there is no objection to the inclusion of the left phrenic nerve with the scar that is removed, thereby resulting in a paralysis of the left side of the diaphragm.

As has been said, the regular rhythm of the heart may be disturbed by the operative procedure. This is particularly likely to occur when traction is made on the scar. Whether or not an irregularity occurs, it is important to allow frequent "rest" periods. During this time, warm moist sponges should be applied to the surface of the heart. Heuer and Stewart have described accurately the alterations in the heart beat in their patients.

"In the 7 patients subjected to operation, the heart beat, as counted at the wrist, varied between 100 and 160 and in all cases was over 130 during the greater part of the operation. In 2 cases the heart action was fairly regular, in 5 markedly irregular. In some cases there were periods of paroxysmal tachycardia, in others transient ventricular fibrillation, in still others such complete loss of rhythm that the cardiac action could be described only as complete arrhythmia. Periods of transient stoppage of the heart occurred not infrequently."

Beck and Mautz (7) recommend the direct application of procaine or metycaine to the heart for the reduction of irritability of the myocardium. There was no effect on the cardiac action in the 1 case in which this method was used by Heuer. Frequent interruptions, allowing the heart to rest, appear to be of the greatest aid in reducing irregularities.

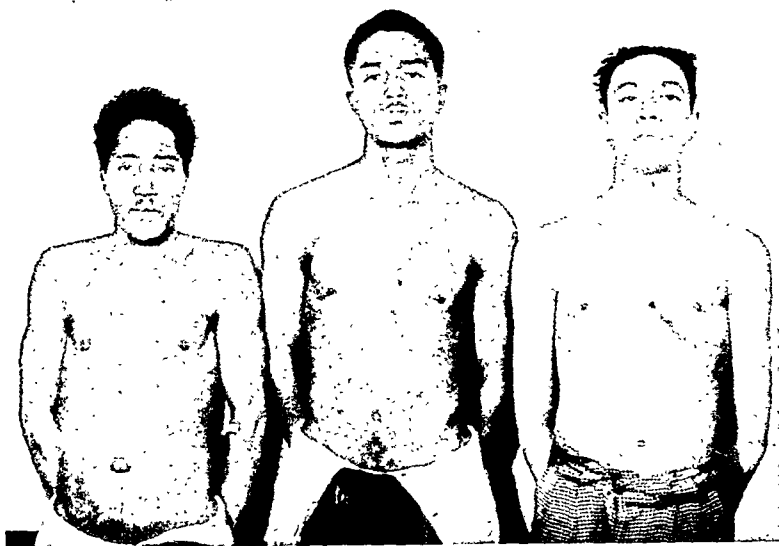


Fig. 12. Showing postoperative photograph taken on February 2, 1937 of patients listed as Cases 1, 2, and 5 in Table II. Patient on left had a healed pericardial scar, subsequently developed tuberculous pericarditis from which he recovered. Operation by Dr. Bigger, second successful case in America. Patient in center had constrictive pericarditis following staphylococcus infection. Organisms still present at time of pericardectomy. Patient on right had tuberculous constrictive pericarditis with activity. This is the only patient on whom we have performed a second operation for the removal of additional scar. The venous pressure is essentially normal in these three patients and fluid accumulation has ceased. Photomicrographs of the scars are shown in the succeeding three figures.

If an opening has been made unintentionally into the left pleura, it is probably just as well to make no attempt to close it. In fact, Griswold recommends that an opening be made deliberately into the left pleural cavity in order that any fluid which forms about the heart may accumulate there, from which site it may be aspirated. This would seem to be unwise in the presence of an active infection and should be used only when there is a healed scar.

*Closure of the incision.* After the decortication has been completed, the skin and muscle flap is replaced over the defect, and the incision is closed. The authors agree with Churchill and Heuer that the insertion of a drain is usually unnecessary and unwise. If there is evidence of an active residual pyogenic infection, a small drain should be introduced.

The danger of tamponade from an accumulation of fluid in the precordial region is not great, since the fluid can pass into the tissue

spaces of the chest wall. It is not as though it accumulated beneath a dense, inelastic scar. If the accumulation of fluid should embarrass the heart's action, it can be aspirated usually without difficulty.

*Postoperative treatment.* A number of surgeons, including Churchill and Harrington, state that all patients following pericardectomy, should be placed in an oxygen tent or cabinet. We agree with Heuer that the inhalation of a high concentration is usually unnecessary unless indications such as dyspnea and cyanosis are present. Blood transfusions should be avoided if possible because of the danger of cardiac dilatation. If blood or other fluids are given intravenously, not more than 30 cubic centimeters per minute should be introduced.

Postoperative treatment consists in the main of a continuance of measures which were used before operation, such as limitation of fluid and salt intake and the use of diuretics when indicated. The accumulation of fluid in



Fig 13 Section of pericardium showing a thickened and hyalinized scar without evidence as to etiological agent. Tuberculous peritonitis demonstrated at subsequent operation.  $\times 10$

serous cavities usually does not stop abruptly and aspiration should be performed when indicated.

#### RESULTS—PROGNOSIS WITH AND WITHOUT OPERATION

Churchill (23) in 1929 collected the reported operations or attempts at operation on patients with constrictive pericarditis. The total number of cases was 37 and the results were as follows: (1) The operation was not completed in 5 patients; (2) there were 7 deaths directly attributable to the operative procedure; (3) there was no improvement in 2 patients who survived the operative procedure; (4) the improvement was transitory in 4 patients who subsequently died of the original disease, and (5) the result was excellent in 19 patients, or 59 per cent of the total.



Fig 15 Case 5. Section showing a thickened scar due to proliferative tuberculous infection. Caseation and giant cells are to be observed.  $\times 10$



Fig 14 Section showing chronic inflammation due to staphylococcus aureus.  $\times 125$

A similar survey of the literature was made by Heuer and Stewart in 1939. They found the reports of 143 patients in whom the pericardectomy had been performed for chronic constrictive pericarditis. Of the 143 patients, 50, or 35 per cent, were reported as cured and 25, or 17.5 per cent, as improved. Nineteen patients died while on the operating table and 28 died in the immediate postoperative period, a total of 47 patients, or 32.8 per cent of the entire number. Thirteen patients died at variable times after discharge from the hospital, 6 of these lived for more than a year and were probably improved by the operative procedure. The 7 remaining patients in this group of 13 died from 2 to 8 months following the operation, probably as a result of the continuation of the disease. The results of surgical therapy were not obtainable in 8 of the cases. Heuer and Stewart state "The final analysis, then, shows that of 135 patients in the reports of whom data are available, 50, or 37 per cent, are cured, 31, or 23 per cent, improved, and 54, or 40 per cent, died, either during or soon after operation." Heuer and Stewart make the additional comment that it should be realized that the 135 cases represent the sum of the experience of 49 observers, 27 of whom have operated upon only a single patient, 7 of whom have operated upon 2 patients, 6 have performed the operation 3 times each, and only 8 surgeons have operated upon 5 or more patients.

The total number of instances in which pericardectomy has been performed is probably at present considerably larger than the 143 cases analyzed by Heuer and Stewart. There are undoubtedly a number of cases that have not been reported. Pericardectomy for constrictive pericarditis has been performed on 20 patients in the Vanderbilt Hospital and probably on a slightly greater number of patients in both the Massachusetts General and Lakeside Hospitals, some of which are unreported. Heuer of Cornell reported last year the results of 7 such operations and Harrington of the Mayo Clinic recently described the results of 9. The previous findings that approximately 60 per cent of the patients are either cured or greatly improved by the operation is corroborated by recent results. Heuer's series is unique in that there have been 7 operations without a death. Three of the patients are cured and 4 are markedly improved.

As in all types of surgery, the mortality rate and the percentage of cures is dependent somewhat upon the etiological agent and the stage of the disease. For example, a comparison of the mortality rate in operations on healed pericardial scars with that in operations on tuberculous processes which are still active is somewhat like comparing the mortality rates in appendicitis with and without peritoneal infection. It is likely that the percentage of disappointing results will always be rather high if pericardectomy is performed on patients with tuberculous constrictive pericarditis without fluid but with activity. The important question is whether pericardectomy in this stage of the disease results in more cures than nonoperative treatment. It should be emphasized that we refer to the stage in which the fluid has disappeared, the venous pressure is rising, the patient is losing ground, and activity is still present. Particular attention is devoted to this aspect of the subject because there is general agreement that pericardectomy is indicated in all instances in which there is a healed scar that is causing incapacitation.

The mortality rate in tuberculous pericarditis, acute or chronic, is extremely high. Harvey and Whitehill analyzed the results in

the Johns Hopkins Hospital, and they state: "Of 20 proven cases with effusion 16, or 80 per cent, died, and 15 of the 17 proven cases without an effusion succumbed, making a total mortality of 83 per cent." Keefer reviewed a series of 20 patients with tuberculous pericarditis at the Boston City Hospital. Of this group, 18 died and 2 survived. The findings of others support these observations. The picture, however, is not as grave as it appears to be. There are undoubtedly a good many instances of mild tuberculous pericarditis in which recovery occurs. A positive diagnosis can be made only by aspiration (with demonstration of organisms), by operation, or by autopsy. Tubercle bacilli cannot be demonstrated in the pericardial fluid in a good many instances of pericarditis which are almost certainly tuberculous in origin. These are the less severe cases in which spontaneous recovery is apt to occur. That a severe infection may result in a healed scar is suggested by this finding in patients with other tuberculous lesions. Granting that these conjectures are correct, the prognosis is extremely poor in a patient in whom tubercle bacilli can be demonstrated in the pericardial fluid. If the acute infection is survived, there results in nearly all instances (13) a constricting mass of tuberculous tissue which may be converted subsequently into a dense scar.

An analysis of the 20 patients in the Vanderbilt Hospital on whom pericardectomy was performed shows that the scar was proved to be tuberculous in origin in 13, that it resulted from a previous staphylococcus infection in 3 and that the etiological agent was undetermined in 4. One of the latter 4 subsequently entered the hospital with tuberculous peritonitis, and the assumption appears warranted that the pericardial scar was tuberculous in origin. The etiological agent could not be determined in a second of these patients because hemorrhage necessitated the abandonment of the operation before any scar was removed. The patient developed pneumonia from which she died, and an autopsy was not performed. Of the 13 patients who had an active tuberculous process in the scar at the time of operation, 7 are living and 6 are dead. Of the 10 who survived the operation for more

than 3 days, 7 are living and 3 are dead. It seems only fair to state that these 3 early deaths were due to the operation and not to the fact that activity was present. Two of the patients in Churchill's series (24) had an active tuberculous pericarditis at the time of operation. He stated: "Both patients died promptly, one on the operating table and the other a few hours subsequently, their lives being shortened a few days as a result of the operative procedure." Again, it is possible that death would have occurred even if the process had been inactive. The 3 late deaths in the Vanderbilt series following pericardectomy for a tuberculous scar occurred 2 months, 6 months, and 2 years following operation and were due to miliary tuberculosis. There is no reason to believe that their lives were shortened by the operation. Harvey and Whitehill found that the average duration of life from the onset of symptoms in 15 patients with tuberculous pericarditis without effusion was approximately 5 months. Pericardectomy was not performed on any of these patients and the diagnosis was confirmed at autopsy. The average duration of the disease in Keefer's 18 fatal cases was approximately 3 months. There is no doubt but that it is better to operate upon constrictive pericarditis due to tuberculosis in the healed rather than in the active stage but our findings indicate that the prognosis is far from being hopeless when it is necessary to operate before all of the activity has subsided.

Three of the 20 patients on whom pericardectomy was performed or attempted had had acute pericarditis due to the staphylococcus some months previously. There were small residual abscess pockets containing staphylococci at the time of pericardectomy. Two of the 3 patients are well 7 and 6 years respectively following the operation. The third patient, a very sick youth with other foci of infection, died 14 days after operation of bronchopneumonia.

There were only 3 patients with a healed scar without activity. One of these, the second successful pericardectomy in America (operated upon by Dr. I. A. Bigger), presented a healed scar at the time of operation but returned subsequently with tuberculous

peritonitis. The latter finding suggests that the pericarditis was also tuberculous in origin. The patient is well at the present time which is 11 years since the operation on the pericardium. It has been 6 years since the operation on the second patient with a healed scar and he is entirely free of symptoms. The third patient, who was operated upon less than a year ago, appears to be well. This small number of cases confirms the opinion of others that the prognosis is better with a healed scar than with an active process.

A postoperative photograph of three patients is shown in Figure 12. At the time of operation, one of these had a healed scar without activity, one had a scar resulting from a staphylococcus infection and activity was still present, and the third patient had constriction from a tuberculous process which was unhealed. These are representative of the three types of disease that we have encountered at operation. Photomicrographs of sections of the scars are shown in Figures 13, 14, and 15.

Pericardectomy was not performed, for various reasons, on 5 patients in whom the clinical impression was confirmed at autopsy. Two of these died within less than 24 hours after having been admitted to the hospital. An active tuberculous process without fluid was found in all cases and it was considered to be the chief cause of death.

An interesting unanswered question is concerned with the reason for the very slow improvement that occurs in many patients following pericardectomy. The prevailing opinion is that the constriction has resulted in atrophy of the heart muscle and that a considerable time is required for a return to the normal condition. This explanation does not suffice in all instances. At any rate, one should not despair if the improvement is slow and if a period of many months is required for the desired decline in the venous pressure and the elevation in the cardiac output.

#### CHRONIC MEDIASTINOPERICARDITIS DIAGNOSIS

Mediastinopericarditis refers to the condition in which fibrous tissue binds the heart firmly to the adjacent tissues including the

rigid structures, ribs and their cartilages, sternum, and vertebral column. The firm attachments of the heart to the neighboring structures frequently results in precordial retraction with each contraction of the heart. This is considered by most observers to be an added burden on the heart, and it may be a factor in the cardiac enlargement and heart failure which occurs not infrequently in these patients. This point is difficult to determine because mediastinopericarditis is usually associated with other abnormalities of the heart.

The type of mediastinopericarditis which may be of interest from a surgical viewpoint usually occurs as a late result of rheumatic fever. Valvular disease of the heart is usually present, and this renders difficult the recognition of the condition in patients and the understanding of the mechanical difficulties of the heart. Burwell (17) states that it is difficult or impossible to separate many of the effects of endocardial and myocardial disease on the one hand from those of pericardial disease on the other. It has been noted frequently that the largest hearts are likely to be found in association with mediastinopericarditis. Since these patients usually have valvular disease as well, it is difficult to assess the rôle played by the two disturbances. This point has been studied by Laws and Levine. They found that the average heart weight of patients with mediastinopericarditis and valvular disease is greater than that of patients with valvular disease only. The average weight of the hearts in the group with mediastinopericarditis and valvular disease was 654 grams while the average of those with valvular disease without pericarditis was 534 grams. This is interpreted as meaning that external adhesions increase the work of the heart.

Even though there are many signs which are said to be of aid, the diagnosis of mediastinopericarditis is a difficult one to make with certainty. The presence of a very large heart with multiple valve lesions should lead one to suspect it. The retraction of the precordial ribs with each systole of the heart is an important point on physical examination. Holt states that systolic retractions of the interspaces are common and without significance, being present when a large heart without ad-

hesions is in direct contact with the chest wall. On the other hand, systolic retractions of the sternum and costal cartilages or of the eleventh and twelfth spaces in the posterior axillary usually indicate adhesions. Fluoroscopic examination may reveal a systolic tug on the diaphragm. Other signs of less value include the diastolic collapse of veins and the diastolic rebound of the chest wall. Fixation of the heart as determined by fluoroscopic and electrocardiographic studies may be of aid in diagnosis. Dieuaide (27) found when the heart is anchored by extensive adhesions that its fixation may be demonstrated by failure of the electrical axis to change to a normal degree with change of position of the patient.

Burwell (17) states that most patients with this type of pericardial disease run a course not very different from that of other patients with chronic rheumatic disease of comparable degree. In patients with mediastinopericarditis without constrictive pericarditis, the main impediment to the heart's action is with systole, not with diastole, and back-pressure with venous stasis is not a prominent finding unless myocardial failure occurs. It should be realized, however, that both constrictive pericarditis and mediastinopericarditis may be present in the same patient.

#### TREATMENT

There is a difference of opinion concerning the value of the several operative procedures in the treatment of mediastinopericarditis. Hosler and Williams agree with Beck in stating:

"In view of our experiments and analysis of autopsy material, we believe that pericardial adhesions in general, and to the diaphragm in particular, do not play a significant role in the production of cardiac hypertrophy. The beneficial results of and the indications for the Brauer operation have probably been over-emphasized in the past."

Bigger (9), on the other hand, is of the opinion that some of these patients are benefited by surgical therapy. He stated:

"The Brauer operation for mobilization of the precordial portion of the chest wall is not indicated often, and some surgeons, notably Beck, have stated that it has no place in cardiac surgery. This hardly seems correct, however, for while adhesions between

the epicardium and pericardium alone do no particular damage, such adhesions when associated with fixation of the pericardium to the chest wall or diaphragm do add a great burden to the heart, producing hypertrophy and dilatation, and eventually failure. Admittedly, such cases are rare, but when correctly diagnosed they may be relieved by this simple procedure."

Even though our experience with this disorder has been quite limited, we are inclined to agree with the opinion of Bigger. A small number of encouraging reports of benefit following the Brauer procedure have appeared in the literature. However, the assertion of Beck (2), that the extra bed rest and attention afforded these patients before and after operation did them more good than the operation itself, has not been disproved.

Even though there is some doubt as to the value of surgical procedures in the treatment of mediastinopericarditis, they will be considered briefly. If fluoroscopic examination shows evidence of dense adhesions between the diaphragm and the pericardium, the left side of the diaphragm may be paralyzed by crushing the phrenic nerve with the hope that an operation of greater magnitude will not be necessary. A temporary paralysis is preferable to a permanent one and it may be made permanent at a subsequent date if improvement follows the initial procedure.

Mobilization of the precordial area is obtained by removing cartilages, ribs, and part of the sternum. Local anesthesia usually suffices for this operation. A satisfactory incision is that which is begun over the third costal cartilage, it is directed downward and medially to the midportion of the sternum, and it ends over the seventh costal cartilage in the midclavicular line. The skin-muscle flap is dissected laterally in order to expose the bony structures. The fourth, fifth, and sixth costal cartilages are the minimum that should be removed, and it is sometimes advisable to include the third and seventh cartilages. A segment of rib, several centimeters in length, should be removed with each cartilage. In order to prevent regeneration, perichondrium and periosteum should be removed with the cartilages and ribs. It is usually advisable to remove a portion of the sternum. Bigger (36) advises the removal of the inter-

costal bundles corresponding to the ribs and cartilages. If it is suspected that constrictive as well as mediastinopericarditis is present, a small portion of the pericardium is exposed and an incision is made into it. If the pericardium is normal, the incision is closed. The skin-muscle flap is replaced and is closed without drainage with interrupted sutures.

#### SUMMARY

Twenty-eight examples of constrictive pericarditis are reported. The alterations of the circulation resulting from this condition are described. The etiology, diagnosis, course, and treatment of the 28 patients are made the basis of a consideration of these aspects of this variety of pericardial disease. For the sake of completeness there is added a brief discussion of mediastinopericarditis.

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# EVALUATION OF INCAPACITY PRODUCED BY INJURIES OF THE PERIPHERAL NERVES

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**T**O evaluate the incapacity resulting from injury of a peripheral nerve, it is necessary, if the evaluation is made soon after the injury, to determine whether the nerve is anatomically severed or only physiologically interrupted; stated in another way, whether it is spontaneously recoverable or not. It is further necessary to determine whether it is completely or only partially anatomically severed. If not severed, but compressed, is it spontaneously recoverable?

If evaluation is made at a later date it is necessary to determine first whether spontaneous recovery has occurred as fully as might be expected and then to measure the residual disability. It then becomes necessary to determine whether operative treatment would be of benefit and to evaluate the probability of recovery. After operations upon the nerve, if seen some time later, it is necessary to determine whether the nerve is recovering and to evaluate the probability of further recovery and its expected degree. Opinion must be based upon the time and character of the operation and pathological condition found.

If, after a sufficient time following the operation, some disability remains, it is necessary to determine whether operative procedures other than on the nerve, such as muscle transplantation, tendon transplants, capsulotomy, may further improve function; and finally, if no further recovery is expected, to determine loss of function. It does not always follow that, because a nerve may not recover, loss of function is permanent. At times, the movements subserved by the injured nerve may be produced by other muscles, for example, almost complete recovery of movement about the shoulder girdle may take place in some cases of irreparable injury to the circumflex nerve.

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In the evaluations of residual incapacity there is found uncertainty, lack of uniformity, and discrepancies between the authors and boards of different countries and of the same country. At times the evaluation has been based upon analogous situations, for example, the loss of function produced in a part of an extremity by ankylosis may be used as an index of the loss of function resulting from an injury of a nerve, thus producing inability voluntarily to move the joint with which comparison is made. Although superior to pure guesses predicated upon which nerve is involved and at what level it is injured, such an approximation does not take into account sensory loss and pain. However, some authorities give quite divergent evaluations for ankylosis of a joint and inability voluntarily to move a joint because of paralysis; Remy, for instance, allows only 20 per cent for an ankylosis at the knee and 40 to 80 per cent for femoral nerve paralysis.

It is obvious that inability to move portions of extremities produces a degree of incapacity which is related to the particular occupation of the patient. A mild sensory loss in the hand would incapacitate a violinist and be non-symptomatic in the case of a ditch digger. To arrive at any accurate tabulation of incapacity, it is necessary to combine the knowledge of neurologists with that of industrial surgeons and boards of compensation. To this the neurologist can contribute the knowledge necessary to determine the degree of injury of a nerve, its recoverability, and the final residual loss of function. Other specialists are necessary to determine the relation of such loss of function to the particular occupation of the patient.

## ANATOMICAL SECTION AND COMPLETE PHYSIOLOGICAL INTERRUPTION

Although many attempts have been made to discover a sign or group of signs which would

justify at a single examination a differential diagnosis between a complete anatomical section of a nerve and one in which complete loss of function is not the result of discontinuity of the nerve but only a physiological interruption, none has been discovered.

Of course, if it is found that only some of the muscles supplied by a nerve are paralyzed or that only a part of the sensory area of the nerve is anesthetic or that the paralyzed muscles contract to stimuli with a faradic current, the nerve is not sectioned.

From a single examination at a particular time, we can determine only whether the lesion is complete or incomplete. If complete we cannot determine at that time whether the nerve is severed or whether its function is totally lost because of some other pathological condition. One cannot predict whether the nerve will spontaneously recover or require surgical treatment.

In a case of complete physiological interruption, only when a subsequent examination shows some return of function may we say that the lesion is incomplete. No other sign or group of signs suffice.

Complete physiological or anatomical interruption both are characterized by a complete paralysis of all of the muscles supplied by that nerve, a complete anesthesia of the isolated sensory supply of that nerve, and a complete reaction of degeneration of all of the muscles it supplies. In addition, many authors have held that the following changes are characteristic of complete lesions: rapid and extensive atrophy of the paralyzed muscles; absence of pain on pressure applied to the nerve trunk below the lesion; marked atony of the muscles; absence of any pain on pressure of the muscles supplied by the nerve; exaggerated excitability of the muscles to mechanical stimuli; abolition of corresponding reflexes; absence of any zone of hyperesthesia or paresthesia in the region supplied by the injured nerve; and severe vasomotor and trophic disturbances. None of the additional signs or combinations of them allows of a determination of the degree of injury in my opinion. Rapid and extensive atrophy of the paralyzed muscles may be interpreted as meaning a severe lesion only with a number of reservations. Ulnar nerve

lesions as a rule show extensive atrophy whether severe or not. Atrophy is of service only when seen relatively soon after injury. Later it is concealed by replacement by other tissue, fibrosis, etc. Thus in an irrecoverable sciatic nerve lesion the amount of loss of mass of tissue may be 1 per cent, that of a recovering lesion, 17 per cent.

Absence of pain, in instances in which the trunk of the nerve is subjected to pressure below the seat of the lesion, was demonstrable in many of my severe lesions, but quite a number of recoverable lesions showed this as well. On the other hand, not a few irrecoverable lesions showed preservation of pain to such pressure. Only the ulnar, radial, and peroneal nerves are suitable for isolated pressure upon their trunks, and this only in cases in which the injury is proximal to their superficial positions. The hazard of producing pain by pressure upon adjacent structures is too great to make this sign significantly diagnostic; absence of pain on pressure of paralyzed muscles is even less significant. In fact in many cases tenderness to pressure was greater over the paralyzed than normal muscles. Hypotonia is too rapidly masked by fibrosis and other local changes to be of any value. Too little is known of the nature of trophic disturbances to enable us profitably to use them in interpreting the severity of a lesion. Ulceration is common in analgesic areas, generalized atrophy of bone occurs with disuse, hypertrichosis appears under bandages and casts; in fact, these changes can be of value only when judged in the light of other findings. As to the absence of hyperesthesia in the region supplied by a nerve, it may confidently be stated that hyperesthesia regularly appears when sensation to pin prick has returned in an area of nerve overlap in completely severed nerves.

The only positive evidence of a complete interruption of function of a nerve is complete paralysis of all of the muscles it supplies, a complete anesthesia of its isolated sensory supply, and a complete reaction of degeneration of the paralyzed muscles.

Total paralysis of all the muscles supplied by a nerve cannot alone be used as an indication of the severity of that lesion. Particularly is this true of the radial nerve, slight injuries

of which may produce total temporary paralysis.

Motion of segments about a joint does not indicate the integrity of the function of the nerve supplying the muscles ordinarily supposed to move such segments. The degree of preservation of the function of muscles is largely ascertained by an examination of the movements of segments about joints and not by the muscles themselves. The frequency with which more than one muscle may produce a similar movement of the segments about a joint emphasizes the necessity for the use of great care in the analysis of all muscle movements. This care is the more necessary in the study of peripheral nerve lesions because the muscles under consideration may receive their nerve supply from different sources.

The preservation of certain movements the loss of which is supposed to follow particular nerve lesions has been observed for many years. These movements may be caused by a number of factors. Among these may be included the anastomotic supply of muscles from adjacent nerves, movements produced by muscles other than primary movers in this action, movements occurring as the result of mechanical factors producing a change of direction of leverage by shortening and lengthening the tendons and muscles passing over several joints, and slight movement resulting from the recoil of elastic tissue following a movement in a direction opposite to the one desired. It is misinterpretation of such "supplementary movements" which lead to incorrect opinions that complete lesions are partial ones.

It is well known that shortly following a division of a mixed nerve, there is seen a certain area of its sensory supply in which all sensation is lost surrounded by an area in which stimuli by pin prick and extreme degrees of temperature are felt. This sensory dissociation and the subsequent behavior of the two zones led to the formulation by Head and his coworkers of their theory that the sensory mechanism in the peripheral nerves consists of three systems: deep sensibility, protopathic sensibility, and epicritic sensibility. The early return of protopathic sensibility (pin prick

and extreme degrees of temperature) within the area of the anatomical sensory supply of a nerve is due to the overlap of function of adjacent uninjured nerves. This return of protopathic sensibility should never be used as an indication of a partial lesion or a recovering one. Only when sensation is present in the isolated sensory supply of a nerve can the lesion be considered a partial or recovering one. The area of the isolated supply to pin prick of various nerves is the area in which no overlapping occurs.

Corresponding to the area of the isolated supply of a nerve to pin prick is found analgesia to pinching, in my opinion an excellent indication of a severe nerve lesion.

Regarding the electrical changes demonstrated by faradic and galvanic stimulation, it may be said that complete reaction of degeneration is always present in a severe lesion but does not indicate an irreparable one. Of all the changes to electrical stimulation the slowness of the muscular contraction is the only constant phenomenon which can be satisfactorily employed in determining the reaction of degeneration. Polar changes are inconstant and of course it may be expected that response to faradism would be absent frequently even in partial lesions. Especially is this true of patients requiring more than 4 months to recover. Before a year had elapsed following injury reaction of degeneration did not indicate an irreparable lesion but after this period and always after 100 weeks, irreparable lesions show complete loss of any response to any form of electrical stimulation.

Partial and spontaneously irrecoverable lesions of nerves may also occur, for example from lateral notches. Whether these are spontaneously recoverable as in the case of complete section can be determined only by repeated examinations revealing evidence of regeneration.

#### SPONTANEOUSLY RECOVERING LESIONS

The signs of regeneration of a nerve are the manifestations of recovery of function. Chief among these are a return of sensibility in the isolated supply of a nerve, disappearance of reaction of degeneration, and return of motion.

These manifestations differ in appearance and rate of return as to the pathology of the nerve and as to whether recovery is spontaneous or is consequent to surgical intervention. They are dependent upon the condition of the neuraxones. If descending degeneration has been slight or absent and the nerve recovers spontaneously and rapidly one type of course is followed; if resection and suture has been performed another type is observed. If little or no degeneration has followed but a complete physiological interruption has existed for a long time, because perhaps of a constricting band, surgical relief of this morbidity is followed by a regeneration similar in character to that observed in lesions rapidly recovering spontaneously. If descending degeneration is severe or complete and conditions are such that the lesion recovers with no surgical interference, the course of recovery will be very similar to that observed following suture.

Rapidly and spontaneously recovering lesions showed two characteristics: First, in agreement with others (Sherren), I have found that such lesions do not show the dissociation of sensation previously referred to. Here little or no sensibility to pin prick returns before tactile sensation. Both forms of sensation are absent and return together. This in my opinion is due to the fact that the function of overlapping nerves is inaugurated only in the presence of a complete interruption whether it be physiological or anatomical. From 200 peripheral nerve injuries which were incomplete and recovered soon after injury, only 3 were found in which sensibility to pin prick was present and tactile sensibility absent. The return of sensibility to both pin prick and touch followed no definite rule as to its location but was in every instance patchy in character. Second, the return of function did not adhere to any definite rate of progression either as to sensation or motion and often all the muscles innervated by a nerve regained their function suddenly irrespective of their distance from the lesion.

Many cases of complete physiological interruption of a nerve showed the first sign of regeneration at such a time as one would expect it to occur were the nerve divided at the time of injury and sutured. From this time

onward the regeneration progressed exactly as would a sutured nerve. It is reasonable to assume that in this type of severe lesion complete descending degeneration had occurred and conditions permitted the regeneration of the axones. Evidence of regeneration first appeared in from the eighth to ninth month, and it was noticeable that a considerable number of men wounded at about the same time, all began to improve together.

In my opinion this is additional evidence that very great conservatism should be exercised in making a decision for resection and suture in severe lesions of peripheral nerves not recovering within even 7 to 8 months.

The order in which the signs of regeneration appear have been given by Mme. Benisty as follows: (1) Sensory regeneration, consisting of pain when the skin is pinched, pain when the nerve is pressed below the lesion, formication on pressure of the nerve and spontaneous aching in certain muscles; (2) arrest of atrophy and return of tonicity; (3) in some cases return of faradic contractility; (4) disappearance of objective sensory disturbances; and (5) voluntary movements.

As critical an examination of the clinical signs of nerve regeneration is necessary as was seen to be the case with the signs of complete physiological interruption of a nerve. In my experience return of pain upon pinching of the skin was many times the first sign of nerve regeneration, but very frequently was not. Only that return of pain to pinching, which is found in such areas of skin as are outside the influence of nerve overlap, can be used as an indication of the recovery of a nerve. Frequently spontaneous aching and more frequently a sensation of a "different feeling" in an extremity preceded other signs of nerve regeneration. Pain upon pressure of the nerve trunk distal to the lesion was found unreliable.

Tinel's sign, or peripheral formication upon pressure or light percussion of the nerve trunk distal to the lesion, was found to be practically valueless. When a nerve is superficial and pressure may be exerted upon it and it alone, this sign might have some value. Unfortunately, only few of the peripheral nerves have a superficial course and this only for a short distance. Elsewhere other structures may be

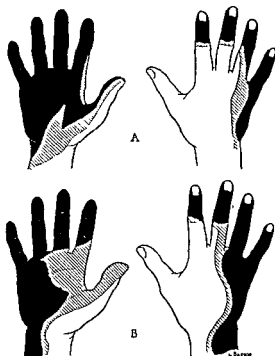


Fig. 2. Sensory loss in complete lesions of the ulnar and median nerves. Black, loss of pain, touch and temperature. Shading, loss of touch.

included in the pressure. When the sign is elicited by light percussion, the concentric waves of motion transmitted from the percussed spot may stimulate the nerve at a considerable distance.

In any event, of 50 cases of recovering lesions, 7 had complete absence of Tinel's sign and 8 had formication for only a short distance from the site of injury. Of 50 irreparable lesions, a complete Tinel's sign was obtained in more than 50 per cent of cases and only in 7 cases was it completely absent.

Arrest of atrophy and return of tonicity were not profitably employed in those nerves recovering some months after injury for reasons already stated.

The electrical phenomena of regeneration of nerves were observed only in those patients recovering more than 5 months after injury. They were not sufficiently critically studied to permit us to use the results obtained in judging the reliability of current views. It may be well to state, however, that in the partial

lesions which showed beginning recovery before the eighth month following injury, a response to faradism at times returned before motion. At times motion was present and faradic response absent. Those showing beginning regeneration following resection and suture, performed not less than 6 months following injury, never showed any return of response to faradism before the return of motion. The same is true of the nerves showing beginning spontaneous regeneration only 8 months or more after the injury.

The early return of sensibility to pain and extremes of temperature in severe lesions of the peripheral nerves and which is attributable to overlap follows a pattern so characteristic that it may be recognized at sight. It never returns in the distal phalanges of the little finger in ulnar nerve lesions, never in the distal phalanges of the index and middle fingers in median nerve lesions, and so on. It always occurs along the borders of an uninjured nerve and may well be described as a shrinkage (Fig. 1).

Contrasted with this, the pattern in recovering nerves is strikingly different. Although shrinkage occurs, other changes are always present (Fig. 2).

The characteristic features of the sensory loss of regenerating nerves may be enumerated as follows: return of sensibility to pain, touch, or temperature sense in that area of the sensory distribution of a nerve which is supplied by it alone, i.e., the isolated sensory area of the nerve; return of sensibility to pain, touch, or temperature sense in patches some distance from the area supplied by an adjacent uninjured nerve; return of sensibility to pain, touch, or temperature sense in deep indentations, diminution of degree of loss of sensation of pain, touch, or temperature sense in the isolated sensory supply of a nerve, return of sensation of pain, touch, or temperature in the border between the sensory supply of two nerves simultaneously injured; interlacing of the border of sensory loss of one type of sensation with that of another.

In the interpretation of the significance of return of motion relative to regeneration, proper recognition must be made of supplementary motility. So great does this influence

the movement of some segments that I have never been able definitely to state that such movements as I have observed return following resection and suture of the ulnar nerve, were due unquestionably to nerve regeneration, with the exception of a distinct contraction of the flexor carpi ulnaris. These movements which cannot be supplemented in the various nerve lesions are:

In musculospiral lesions, extension of the proximal phalanx of the thumb and abduction of the thumb in the plane of the palm, and extension (not alone tension) of the proximal phalanges of the fingers. In ulnar nerve lesions, flexion of the proximal phalanges of the ring and little fingers with the distal phalanges extended, and lateral movements of the extended middle finger. In median nerve lesions, flexion of the distal phalanx of the index finger and of the thumb. In combined lesions of the ulnar and median nerves, all movements of the hand except flexion at the wrist and hollowing of the hand. In external popliteal lesions, eversion of the foot.

Some signs of complete motor recovery are of value: In the musculospiral nerve, placing the little finger on the seam of the trousers with the fingers well extended and with the palm turned to the front, is a sign suggested by Pitres. In ulnar nerve lesions, he suggests that the palm be placed flat upon a table with the fingers apart, then the middle finger should be moved inward and outward and finally the table scratched with the nail of the little finger without moving the wrist. In median nerve lesions Claude suggests the clenching of the fist with all the fingers well flexed into the palm and with the distal phalanx of the thumb firmly pressed upon the dorsal aspect of the second phalanx of the middle finger.

It has been observed by Mme. Ath. Benisty that following individual nerve lesions, certain muscles recover motility in a definite order. In a general way, in our experience, the spontaneous recovery showed this same characteristic: In musculospiral lesions the extensors of the wrist were the first to recover, followed by the extensors of the fingers, then the abductor and extensor of the thumb. In ulnar nerve lesions the intrinsic muscles of the hand were the last to recover. In median

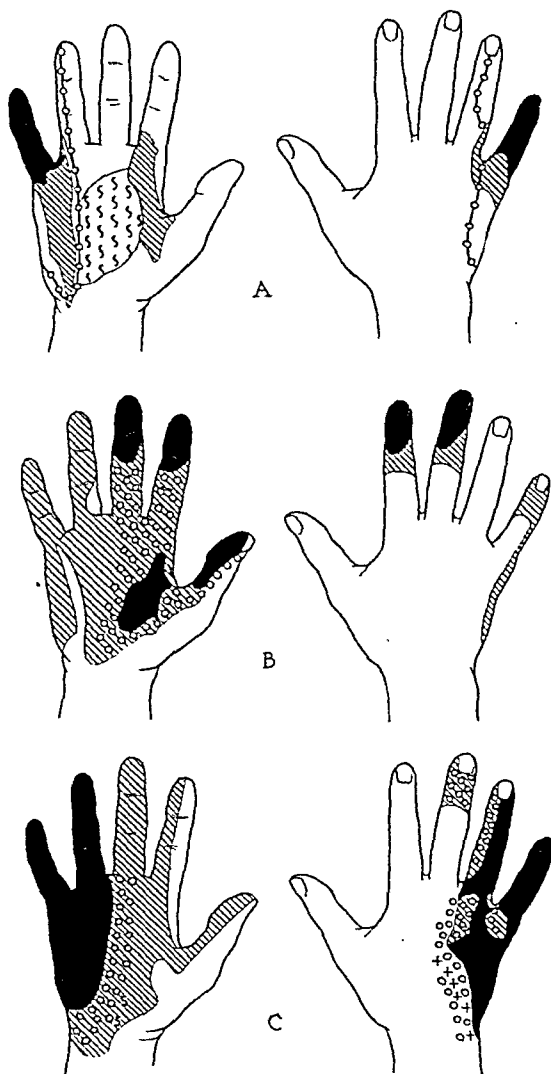


Fig. 2. Sensory loss in recovering lesions of the ulnar and median nerves. Black, loss of pain, touch and temperature. Shading, loss of touch, temperature. Letter S, hypesthesia. Letter X, analgesia.

nerve lesions, the muscles of the thenar eminence and the flexor of the index finger were the last to recover. In external popliteal lesions the extensors of the toes and in sciatic nerve lesions the tibialis posticus and the flexors and extensors of the toes were the last to recover.

Recovery following primary and secondary suture did not always take place according to

a definite rule. I have observed only 39 such cases and among them the first return of function occurred in the following muscles: In musculospiral lesions following primary sutures, the extensors of the wrist, the extensor communis digitorum and abductor pollicis, followed by the extensor longus pollicis; following secondary suture, extensors of wrist, followed by the extensors of the fingers, then the thumb. In median nerve lesions following secondary suture, the pronator radii teres, the palmaris longus, and flexor carpi radialis were the first to recover. The supplementary movement in ulnar nerve lesions was so extensive that it was not profitable to attempt to determine what muscle regained its function first. In combined lesions of the ulnar and median nerves, the flexor carpi ulnaris, flexor longus pollicis, and flexor sublimis digitorum were the first muscles to function following secondary suture. In the external popliteal nerve the peronei, tibialis anticus, extensor longus digitorum, and extensor hallucis were the muscles to recover function first, in the order named, following primary suture. Following secondary suture function in the tibialis anticus and extensor longus digitorum returned first. In the sciatic nerve, following primary suture, the peronei and the extensor longus digitorum were the first to recover function.

Following primary suture the first return of motion was observed in 6 months in musculospiral lesions. The first return of motion in external popliteal cases was observed in 7 months, and in sciatic nerve lesions, in 6½ months, following primary suture. In musculospiral lesions following secondary sutures, the first return of function occurred from 5 to 6 months after suture. In secondary sutures of the sciatic nerve the first return of function was apparent in 6½ months. In external popliteal nerves, the first return of function occurred in 8 months following suture. In a combined ulnar and median nerve lesion, muscles innervated by both nerves showed return of function in a little over 6 months following secondary suture.

When function is considered to be spontaneously recoverable it is necessary to know the expected chances of recovery.

In severe lesions, not anatomical sections, recovery occurred in 21.8 per cent of Wexburg's cases and improvement in 30.4 per cent. Foerster reported 60 per cent of 1,320 cases as recovered, 30 per cent improved, and 10 per cent unimproved. Herzog reported 9.4 per cent recovered and 72.7 per cent improved in lesions of the upper extremities, and 6 per cent recovered and 24.2 per cent improved in lesions of the lower extremities. The duration of the time of recovery may be quite long. The longer it takes for recovery to begin, the less perfect will recovery be, but recovery may begin as long as 2 years after injury and good results may be obtained. In spontaneously recovering lesions it is therefore necessary to wait at least 2 years before final adjudication should be made of irrecoverability.

For spontaneous recovery, the most favorable prognosis may be given in the following order of nerves: tibialis, median, musculocutaneous, axillary, ulnar, radial, peroneal, and sciatic. The most rapid recovery had been observed in the following order: radial, musculocutaneous, peroneal, tibial, median, ulnar, sciatic, axillary.

Following operation it is necessary to have some idea of the prognosis, depending on the particular operation, suture, neurolysis, or transplant, and the time between the injury and operation, such as primary and secondary suture or other procedure. Reports of recovery after secondary suture are so variable as to be interpreted with great difficulty because of the many factors involved and the different standards of recovery time of the reports.

Foerster reports 3 per cent failures in 370 cases; Stracker reports 25 per cent failures in 147 cases; Ranschburg, 64.3 per cent failures in 414 cases; Forrester-Brown, 50 per cent failure; Delagénière reported complete success in 85.9 per cent, partial success in 11.2, and failure in 3 per cent. Stopford described the results of secondary suture accurately and was able to examine his cases for a long time after operation. In 245 cases there were 30 failures; however, a number of cases in which only a return of protopathic sensibility had returned were included among the successes. Platt reported 150 cases of suture with recovery in 79 per cent.

The results of suture differ with individual nerves. Following suture, in a composite material of 6 German authors, failures were reported in 62 per cent of peroneal nerve suture—152 cases; 54 per cent of tibial—67 cases; 43 per cent of ulnar—228 cases; 31 per cent of median—198 cases; 30 per cent of sciatic—121 cases; 28 per cent of radial—397 cases; 21.4 per cent of axillary—18 cases; 18 per cent of musculocutaneous—33 cases.

The interval between the time of suture and injury is of some prognostic significance. Thus Stracker reported that of 21 cases in which operation was done within 3 months after injury, success resulted in 66 per cent; in 4 to 6 months—46 cases, 50 per cent; in 7 to 22 months—69 cases, 24 per cent.

Stopford believed that a delay of from 12 to 18 months appeared to have no marked effect upon the time or extent of recovery. If the interval exceeded this period the prognosis was not so good when the suture had been performed in the distal part of the limb. When in the proximal part a delay of 2 to 3 years does not seem to prejudice the chance of success.

It has seemed to many authors that primary suture results in relatively rapid and constantly favorable results, with which I agree.

Following neurolysis, successful results followed in 77.2 per cent of Foerster's 194 cases; in 37.2 per cent of 405 cases reported by Ranschburg; in 75 per cent of 80 cases reported by Platt.

Homoplastic and heteroplastic transplants have been uniformly unsuccessful. Of 216 cases analyzed by Gossett and Charrière, in only 5 were good results seen in autografts, 2 in homografts, and 5 in heterografts.

When after a sufficient time has elapsed following operation,  $2\frac{1}{2}$  to 3 years, to enable one to say that there will be no further recovery, other operative procedures should be contemplated, such as arthrodesis, tendon and muscle transplants, and similar procedures. Only when no more favorable results may be expected should the final evaluation of incapacity be made.

McBride suggests that the disability be measured in terms of loss of abduction, adduction, flexion, extension, and rotation. The

disability then is approximately the same as in the presence of ankylosis. This suggestion has many merits and is far more sensible than the guesses arrived at by some. If in addition, the examiner bears in mind the extent of sensory loss as well as the type of occupation of patient, with the idea of determining what function required by that or allied occupations has been destroyed, he will be able to make a fairly accurate approximation of loss of function.

Kessler has properly noted that the estimate of permanent disability is often made at the time patient returns to work regardless of whether the nerve might regenerate further. Thus in one instance, a musculospinal lesion, patient was awarded a 30 per cent loss of function; later, however, complete recovery took place. As has been pointed out the beginning of recovery may be delayed in spontaneously recovering nerves as long as 2 years and in sutured nerves as long as  $2\frac{1}{2}$  to 3 years. For future reference and further to emphasize the difference of opinion concerning evaluation of incapacity produced by paralysis in various nerves, it may be of interest to note the evaluations from several sources.

Injury to the whole brachial plexus is awarded by Kaufman, when on the right side 75 per cent, on the left side 65 per cent; the *guide barême*, on the right, 70 per cent, on the left, 60 per cent. Injury to the upper part, or Erb's palsy, is awarded by Imbert 20 to 25 per cent; by *guide barême*, 20 per cent on the right, 10 per cent on the left; by Llewellyn, right 25 to 30 per cent, left, 20 to 25 per cent. Injury to the lower brachial plexus or Klumpke-Déjerine paralysis, is awarded by *guide barême* 30 per cent on the right, 20 per cent on the left; by Llewellyn 35 to 40 per cent on the right, 25 to 30 per cent on the left.

For injury to the suprascapular nerve, Llewellyn awards 10 per cent when external rotation is important; *guide barême* 30 per cent on the right and 20 per cent on the left. The subscapularis is awarded 10 to 15 per cent by Kessler. For injury to the circumflex nerve Llewellyn awards 25 to 30 per cent; *guide barême* 20 per cent on the right, 10 per cent on the left; Imbert 20 to 25 per cent; Remy 15 per cent on the right, 12 per cent on the left;



Thieme 60 per cent on the right, 50 per cent on the left; Kaufman 15 to 20 per cent; the Swiss authorities, 15 to 20 per cent; Mayet 20 per cent.

The long thoracic is awarded 15 per cent by Kaufman

The musculocutaneous is awarded 30 per cent by Mayet; the *guide barême* awards 50 per cent on the right, 40 per cent on the left; Llewellyn likewise gives 50 per cent on the right and 40 per cent on the left for complete lesions and 30 per cent on the right and 20 per cent on the left for incomplete lesions; Kessler gives 60 per cent

When the musculospinal is injured above the triceps, Mayet gives 50 per cent, below it, 40 per cent. When in the arm Remy gives 60 per cent on the right, 10 per cent on the left as does Imbert. The *guide barême* awards 60 per cent on the right, 50 per cent on the left, generally the German authorities give from 40 to 60 per cent. When the hand alone suffers from the paralysis Thieme gives 50 per cent on the right and 45 per cent on the left; Remy 50 per cent on the right and 48 per cent on the left; and Kaufman 50 per cent. Kessler gives 66 per cent on the hand.

For median nerve lesions above the innervation to the flexors of the wrist and fingers, the *guide barême* gives 50 per cent on the right and 40 per cent on the left, as does Remy; Imbert gives 45 per cent to 50 per cent, Llewellyn gives 60 per cent on the right, 50 per cent on the left; Thieme from 40 to 50 per cent. When involving only the small hand muscles, Remy gives 45 per cent on the right and 35 per cent on the left, and Imbert gives from 15 to 20 per cent. Kessler gives 40 to 70 per cent in the arm, 10 to 20 per cent in the hand. For causalgia Llewellyn gives 80 per cent on the right, 70 per cent on the left. For lesions of the ulnar nerve Kessler gives from 15 to 60 per cent below the elbow, 45 to 60 per cent above the elbow, 20 to 60 per cent at the elbow, in terms of hand disability; the *guide barême*, at the elbow 50 per cent on the right, 40 per cent on the left; Remy in the hand 12 per cent on the right, 10 per cent on the left, Thieme above the hand 55 per cent on the right, 50 per cent on the left; Mayet, 30 per cent above the elbow, 20 per cent below the

elbow; Llewellyn, 50 per cent right, 40 per cent left, and at the wrist, 25 per cent on the right and 30 per cent on the left.

The sciatic nerve is awarded 60 to 70 per cent by Llewellyn; 60 per cent by Imbert; the German authorities generally, 40 per cent; but although Remy gives 40 per cent he thinks 60 per cent is not excessive.

The peroneal nerve is awarded 10 per cent by Remy; 20 per cent by the *guide barême*; 30 per cent by Llewellyn, 40 per cent by Golebiewski (quoted by Imbert).

The tibial nerve is awarded 20 per cent by Llewellyn.

The femoral nerve is awarded 50 to 60 per cent by Llewellyn; Imbert gives it 40 to 50 per cent; the German authorities generally, 66 to 85 per cent; the *guide barême*, 45 to 50 per cent.

The wide difference of opinion held to be authoritative is immediately apparent and often ludicrous. As Llewellyn has pointed out, to determine disability by the level of a lesion and not by actual paralysis present is certainly erroneous. If the level of the lesions is to be considered then the level should be related to the branch of the nerve above which it is located.

For ankylosis at the knee Imbert awards the same as for amputation, 60 to 65 per cent; Remy gives it as 20 per cent; Brouardel, 20 to 60 per cent according to occupation; Llewellyn, 25 to 45 per cent. If a brace is cumbersome, an arthrodesis can produce an ankylosis at the knee when the femoral nerve is injured and function will be equally as good as when the nerve is not injured, yet the German authorities give as high as 85 per cent for paralysis of the femoral nerve, and Remy, on the other hand, gives 20 per cent for ankylosis at the knee.

Thus, whereas much is known of methods of determining the recoverability of nerves, the probabilities of recovery after operation, residual paralysis, and anesthesia, possible supplementary movement, and methods of improving function, much remains to be learned concerning the estimation of incapacity as related to industry, arts and professions, produced by loss of function resulting from peripheral nerve lesions.

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# THE DIAGNOSIS OF CHRONIC ENLARGEMENT OF THE LEG

## With the Description of a New Syndrome

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**T**HE subject of chronic enlargement of the leg is an interesting one chiefly from the standpoint of diagnosis. Scattered descriptions of all but one of the various conditions to be described have appeared in the literature, but there has been little organization of information, and I have been unable to find any writings which deal with the subject in regard to differential diagnosis. It is my aim to discuss this condition so as to present a guide in the investigation and diagnosis of a case of chronic enlargement of one lower extremity. I also wish to present the description of a hitherto unreported syndrome of leg enlargement. The treatment of the majority of these conditions is unsatisfactory and far from standardized, and, because I have little that is new in this respect to offer, treatment will not be considered in this article.

Unfortunately, cases of leg enlargement are seen most frequently in the female sex, and consequently the majority present themselves primarily for cosmetic reasons. In this age of silk stockings, short skirts, and glamour, one enlarged leg is a serious handicap from the psychological standpoint, even without taking into account the symptoms produced. The male sex undoubtedly shows a lower incidence of this disablement despite the fact that the cosmetic reason is negligible. The main reason for the preponderance of females is that the two groups showing the greatest number of cases, the pure lymphatic and the lymphaticovenous types, occur most commonly in females, the latter being so often a complication of pregnancy.

As there are numerous causes for the development of an enlarged leg, the subject will be discussed under the following headings: (1) congenital hypertrophy; (2) lymphatic stasis and obstruction, congenital and acquired, (3) developmental venous retardation, (4) mixed

venous and lymphatic partial obstruction; (5) congenital arteriovenous fistulas; (6) miscellaneous.

### CONGENITAL HYPERTROPHY

This group includes only those cases of enlargement of the limb due to congenital overgrowth. All the component tissues of the leg are otherwise normal. There are other congenital causes for leg enlargement, but they will be discussed under their appropriate groups.

In the symmetrical development of the two sides of the body it is somewhat surprising that unilateral differences do not occur more frequently. Congenital anomalies are relatively frequent, but major variations in symmetry are rare. One manifestation of unilateral inequality is an enlarged leg. Many isolated case reports of congenital hypertrophy have appeared, and Wakefield and Hines have collected a series of 223 cases. However a careful perusal of these reports demonstrates that many of them are not true congenital hypertrophies, but are either congenital lymphedemas or congenital arteriovenous fistulas. As this latter syndrome has not been really understood until recently the difficulties in differentiation can be understood. While congenital hypertrophy undoubtedly occurs, it is not as common as was previously believed.

In another contribution to the subject, Braggman lists 4 different types of congenital hypertrophy. (1) unilateral total hypertrophy; (2) unilateral hypertrophy of one extremity; (3) crossed hypertrophy of one leg and the opposite arm; (4) individual organ hypertrophy. It is only group (2) pertaining to the leg which concerns us in this discussion.

For the diagnosis of a case of congenital hypertrophy it is essential that the history shows that the defect was noticed at birth or shortly afterward. Enlargements appearing in later life are not congenital hypertrophies. In unilateral total hypertrophy, and in crossed

hypertrophy, the diagnosis is obvious, but when only one leg is involved the diagnosis must be made by exclusion. To be able to make the diagnosis in such cases, the examiner must have in mind a clear conception of the other congenital causes leading to enlargement of the leg. These will be dealt with subsequently. An aid in confirming the clinical impression of congenital hypertrophy is the frequent finding of other congenital defects, such as spina bifida, club foot, cleft palate, etc. and later evidence of mental deficiency. Prolonged elevation of the leg results in no change in size.

#### LYMPHATIC STASIS AND OBSTRUCTION

This group may be subdivided into congenital and acquired varieties, and it gives the second largest number of cases of enlarged leg.

*a. Congenital.* There is some confusion in nomenclature in this group. The true congenital leg enlargement due to lymph stasis is known as Milroy's disease, but to be correctly placed in this category there must be a definite familial incidence.

Milroy emphasized the familial tendency and reported the lesion present in 7 successive generations in his series. Descriptions of other similar families have appeared, but most cases will not give a familial history, and are therefore more correctly designated as congenital lymphedema.

The basic factor underlying this condition is a developmental defect in the lymphatic system of the lower extremity resulting in a diffuse lymphangiomatosis with lymph stasis. This is localized in the area between skin and fascia. The clinical picture presented is that of an enlarged leg which is slightly paler than the other and which demonstrates a slight pitting edema more marked toward the end of the day. That edema is the factor concerned can be proved by continued elevation of the leg for 24 hours, when the limb will be observed to be diminished in size, more nearly approaching the normal extremity. There is no increase in length of the involved leg, no increase in warmth, no dilated superficial veins, and no ulceration or angiomas. The child appears perfectly normal except for an enlarged leg. The history in these cases must be that



Fig. 1. Lymphedema precox involving the left lower leg most marked about the ankle, but also extending slightly above the knee.

the defect was noticed at birth or shortly afterward. Although the case usually can be diagnosed clinically, when in doubt, biopsy of the skin and subcutaneous tissue will settle the question. The sections will show a spongelike appearance of the subcutaneous tissue with marked increase in the skin to fascia interval. Microscopically there will be seen a replacement of the majority of the subcutaneous fat by widely dilated lymph spaces. These spaces increase in amount toward the deep fascia. There is a varying amount of fibrous tissue present about the lymphatic channels, and especially marked as a thickening of the subcutaneous fibrous septa and the deep fascia. The lymph spaces are lined by a single layer of endothelium and are seldom larger than 2 millimeters in diameter. The microscopic appearance is entirely characteristic.

*b. Acquired.* There is a variety of lymphedema which probably should be grouped in the congenital section, but, because of its late development, will be classified as acquired. This is the spontaneous development of a leg swelling, starting usually about the ankle, which progresses upward slowly, and within a year usually involves the leg to the level of the knee or higher. This condition is most common in females and develops as a rule in the late teens. It has been well described by Allen who has given the syndrome the name of lymphedema precox. In a study of 93 cases

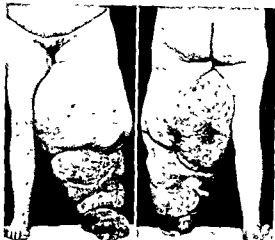


Fig. 2 A severe case of elephantiasis (acquired lymphoedema) following upon successive attacks of cellulitis of the leg. The hyperkeratosis, skin excrescences, edema, and pigmentation are obvious. This leg on amputation weighed 67 pounds (Courtesy of Dr. D. G. Webster).

he found that females preponderated by 87 per cent. It usually involves one lower extremity and is aggravated by prolonged standing and activity. Figure 1 shows a moderately well developed case in a girl aged 19, the enlargement being noticed 1 year previously. The complaints, as in this case, are mainly cosmetic in basis, with the addition of some heaviness and tiredness after prolonged periods of time on the feet. Clinically and pathologically lymphedema precox presents the same picture as that of congenital lymphedema, with the exception of its later appearance.

In 1930 Reichert described an accessory method of diagnosis of edematous extremities by the use of soft tissue x-rays. In lower extremity edema due to generalized causes such as cardiac, nephritis, and hypoproteinemia, the enlargement is shown to be mainly confined to the subcutaneous area but present also throughout all the strata of the leg, whereas in lymphatic stasis and obstruction the enlargement is confined to the skin-fascia interval alone. In most cases a differentiation between the enlargement which is the result of congenital lymphedema and lymphedema precox against that which is the result of chronic lymphangitis can be made, when, in the latter, a marked subdermal diffuse fibrosis can be



Fig. 3 A moderately advanced case of acquired lymphoedema of the same etiology as that portrayed in Figure 2 (Courtesy of Dr. L. P. Ercaux).

seen, manifested as a network of fibrous trabeculations in the subcutaneous interval.

A second variety of acquired lymphedema is that which results from the partial or complete obliteration of the normal lymphatic pathways, and it is to this group that the true cases of elephantiasis belong. This obliteration is the result of moderately severe or recurrent mild attacks of cellulitis and lymphangitis, the organism being predominantly the streptococcus. These attacks result in a progressive edema, fibrosis, and enlargement of the leg by involvement of the extrafascial tissues, the result of chronic inflammation and the fibrous obliteration of the lymphatics both far and near.

The appearance of the leg differs markedly from that of lymphedema precox. The size is usually greater and may be tremendous. Figures 2 and 3 show two good examples of the severe and the ultimate stages of the condition. In both, the result is due to waves of subacute cellulitis and lymphangitis progressing for more than 5 years. Both were natives of Montreal and repeated examinations for filaria were negative. The skin shows a marked thickening and loss of elasticity, and in severe cases like those pictured here, there are patches of hyperkeratosis, pigmentation, and wart-like excrescences. The enlargement may be such that the skin bulges in hard folds with deep creases between. There is always a hard pit-



Fig. 4. This patient has had varicose veins for the past 30 years, but the enlargement of the leg followed an abrasion to the left shin. (The scar of this can still be seen.) The abrasion healed very slowly, and was associated with many attacks of subacute inflammation. This case is one of mild acquired lymphedema with pre-existing varicose veins.

ting edema present which is reduced somewhat on prolonged elevation. The hardness of the tissues is characteristic. There is usually a patchy slight increase in warmth of the involved, over the uninvolved, leg because of the subacute inflammation present in various areas. Leg ulcers are seldom present. The finding of associated varicose veins should not lead the diagnosis astray, such as the case pictured in Figure 4. This man has had veins the size of those present in the photograph for the past 30 years. Eleven years ago he had an abrasion to his lower leg and ever since has had attacks or waves of redness, tenderness, and increasing swelling of his leg. Chills were present on a few occasions. This is an example of a milder degree of chronic lymphatic obstruction. The classical example of this variety of leg enlargement is that seen in filariasis in which the elephantiasis is not caused merely by the presence of the filaria in the lymphatic vessels, but mainly by the lymphangitis which results from their invasion.

Matas and Homans have given excellent descriptions of the whole process, and have shown that mere interruption of lymphatic pathways is not enough to produce lasting edema, but for the edema to be continuous an added chronic or recurrent lymphangitis must be present.

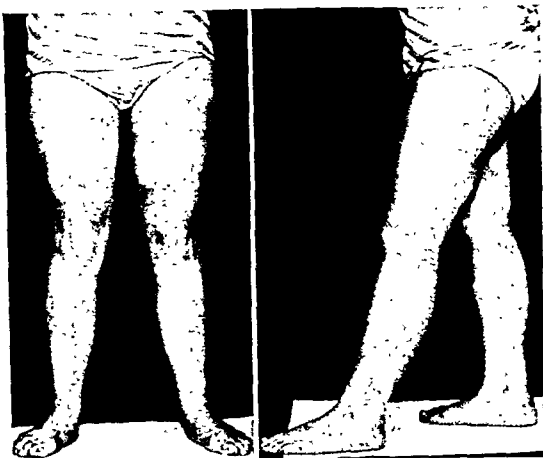


Fig. 5. The case of congenital venous retardation described in the text, showing the slight but definite enlargement of the left leg. There is a generalized patchy cyanosis best seen in the upper thigh and ankle.

The microscopic picture of a section of skin and subcutaneous tissue demonstrates the combined appearance of lymphedema and chronic inflammation. The epidermis is seen to be hypertrophic and may be thrown into irregular folds. There are varying degrees of papillary excrescences and hyperkeratinization. The corium is fibrous and from it fibrous bands extend down through the subcutaneous tissue. The blood channels are thickened and surrounded by a perivascular exudation of lymphocytes. The fibrous tissue is loosely arranged and appears edematous. In severe cases the picture may simulate a myxomatous lesion.

#### DEVELOPMENTAL VENOUS RETARDATION

Pure venous retardation as a cause of leg enlargement in a previously unaffected leg has not been described to date. In other cases in which increased leg size has the factor of retarded venous return, there is also partial lymphatic blockage. This combination is well known and follows on a previous deep thrombophlebitis. This combination and its diagnosis will be discussed subsequently under group 4 as the lymphaticovenous group.

First of all I wish to present a case which in my opinion demonstrates that venous retardation can be a cause in itself of leg enlargement.

A.C., Hosp. No. 111,154, female aged 21 years, presented herself because of an enlarged left leg



Fig 6

Fig 7

Fig 6 Roentgenograms of the case shown in Figure 5 following injection of 70 per cent diodrast solution into the left femoral vein at the level of the groin. The retrograde filling of the entire femoral vein and tributaries is well seen. The large caliber of the vein and the smooth walls indicate the absence of any previous deep phlebitis.

Fig 7 Injection of the right femoral vein at the level of the groin in the same case as that shown in Figures 5 and 6. Note that the diodrast solution does not descend farther than the first valve station.

which was first noticed 1 year ago. There were no associated symptoms until about 2 months before admission when she noticed that in the afternoons, after being on her feet all day, she would have a dull aching pain throughout the entire length of the leg. The leg would be slightly larger in the evenings than the mornings but there has been no return to normal size at any time since the onset.

The patient gives no familial history of enlargement of the leg. She is married but has had no pregnancies. Before her marriage she was a waitress for 2 years. There is no history of accident to the leg or phlebitis, and she has had no operations or serious illnesses.

There were no findings in the general physical examination relevant to the local condition. The left

leg showed a mild generalized enlargement in comparison with the right (Fig 5). Even in the supine position, and much more marked when erect, the left leg showed a definite cyanotic mottling which seemed to be most marked on the lateral aspect of the mid thigh and again in the region of the medial malleolus. There were no varicose or unusually dilated superficial veins present, no nevi or areas of pigmentation, no pitting edema. The skin texture and the feel of the subcutaneous fat were normal.

The arterial pulsations were normal in both feet and legs. Measurement of the extremities revealed equal length, but demonstrated the enlargement on the left side to be due to an increase in circumference of 1 inch in the thigh and  $\frac{1}{2}$  inch in the lower leg. Skin temperature readings by means of the derma-

therm were essentially equal on both legs. Routine urine and blood Wassermann examinations were negative. Soft tissue roentgenograms made of both legs showed the bones to be normal in contour and length, and the enlargement of the left leg to be composed chiefly of an increased thickness of the subcutaneous tissues. There was no arterial calcification or localized zones of soft tissue increase.

The femoral vein on the left side was injected with 70 per cent diodrast solution, the technique being as follows: Venipuncture was performed just below the inguinal ligament with the patient lying on the x-ray table. An assistant then compressed the femoral vein and artery against the superior ramus of the pubis. The injection was carried out without undue pressure, the 30 cubic centimeters being given in about 30 seconds. The proximal digital pressure was continued until the roentgenograms had been taken, and the whole procedure was completed in about 2 minutes. This same procedure was carried out subsequently on the normal leg. The x-ray results are shown in Figure 6 in which it will be seen that the solution descended retrogradely almost the full length of the deep veins in the involved leg and also into many of the tributaries, but there was no reversal of flow in the great saphenous vein. The injection into the femoral vein on the normal side was halted within an inch and a half from the point of injection (Fig. 7).

The conclusions in this case are based on the following points: This patient gives no history of any previous leg disorder, she has never had phlebitis, pregnancy, or any severe illness. There is no familial history, and the enlargement has gradually appeared in early adult life, a time when the equivalent state of defective vein valves in the saphenous systems usually makes its appearance. Edema as an important factor in the enlargement can be ruled out by the absence of pitting on pressure, and only the slight diminution in size on prolonged elevation. There were none of the signs of a congenital arteriovenous fistula present. The diffuse cyanosis of the leg, most marked on standing, indicates a venous congestion; and the lack of enlarged superficial veins rules out incompetency of the saphenous system, although this will probably develop later.

The x-ray studies corroborate the clinical impression by revealing the absence of, or defective valves in, the deep system of the involved leg, thus allowing complete retrograde flow. This defect is absent in the normal leg, the injection being soon halted presumably at the first valve station. This phenomenon of retrograde flow has been present on x-ray in

2 other patients who had had a previous thrombophlebitis, whereas 2 normal controls again showed the injection fluid to penetrate a short distance down the vein. The leg hypertrophy is probably the result of venous retardation and increased venous pressure acting over a long period in a dilated deep venous bed. Undoubtedly this extremity has been endowed with a set of valves congenitally weaker, and likely numerically fewer, than the normal, and the preceding years of activity while a waitress produced their complete defectiveness.

#### MIXED LYMPHATIC AND VENOUS PARTIAL OBSTRUCTION

As before mentioned, to this group belongs the largest number of cases. The leg enlargement is usually only a secondary complaint with the exception of the ankle edema which appears toward the end of a day of activity. It is most commonly the complications which bring these cases for treatment. The underlying pathological condition is that of a thrombophlebitis of the deep femoral system which in many cases progresses well up into the iliac veins. This is an infective phlebitis following pregnancy most frequently, but seen also in septicemia, pneumonia, typhoid, and after operation in septic cases. This thrombophlebitis is always associated with a periphlebitis, a point which can be demonstrated at a later date when some operative procedure on the veins is carried out. Instead of the usual fine areolar tissue surrounding the vein, thick fibrous bands will be found closely binding the thickened whitish vein to the surrounding tissues. This periphlebitis results in a lymphangitis due to the close anatomical association of the lymphatics with the veins, especially in the region of the external iliac vein. Subsequent recanalization of the vein in part is almost invariable, but the action of the valves has been destroyed.

A careful history taking is important in determining a previous deep thrombophlebitis. Such a case will give a history of an acute leg involvement associated with pain, blueness, tenderness, a sharp febrile course, and, especially, marked swelling of the whole leg. These patients will have been in bed for from 4 to 8 weeks and will have been treated usually by



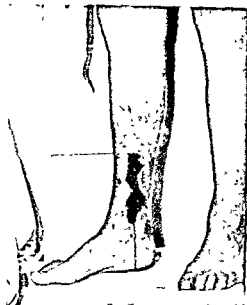


Fig 8 A case of mild enlargement of the right lower leg following a femoral thrombophlebitis associated with childbirth 14 years before. The common complication of ulceration of the lower leg is present.

elevation and hot fomentations. Such a history will distinguish a deep phlebitis from the superficial vein involvement; in the presence of the latter, localized pain and tenderness, mild or absent fever, and little or no ankle edema will be elicited.

The diagnosis of this variety of leg enlargement presents few difficulties. The history of a previous deep thrombophlebitis is of paramount importance. The clinical examination reveals only a slight increase in size of the involved leg over the normal one. This is always more marked toward evening after a day of activity, especially about the foot and ankle. The leg is only slightly larger than its fellow and the most marked tissue changes are in the lower half of the lower leg. The skin in this region is indurated and usually pigmented, and the subcutaneous tissues show a distinct firmness even to the point of hardness. There is no increase in warmth unless secondary infection from complications is present (Fig 8). The arteries pulsate normally. The appearance of the lower leg will be modified by the frequent complications of eczema and ulceration which ensue. Contrary to the popular belief, it is

the exception for a case of deep femoral phlebitis to develop subsequent incompetent superficial varicose veins. Careful questioning will reveal that when varicose veins are present, they were in existence before the onset of the deep phlebitis and probably were a factor in its development.

#### CONGENITAL ARTERIOVENOUS FISTULA

This variety of leg enlargement is one of unusual interest. It consists of a hypertrophy of all the component parts of the leg the result of abnormal arteriovenous communications of congenital origin. As would be expected, the majority of cases develop in early childhood, but there are some which do not make themselves evident until later in life probably because of the small size of the fistulas at birth. As growth and activity continues these small fistulas enlarge to the point of producing signs and symptoms. To obtain a hypertrophied leg in a case of arteriovenous fistula, the communications must be well above the knee. The level of the fistula will determine the amount

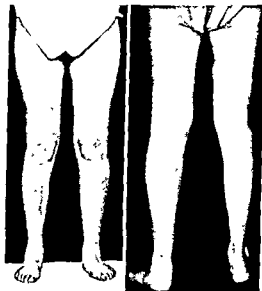


Fig 9 a, left, Case of congenital arteriovenous fistula involving the vessels in the left thigh, and showing the generalized enlargement of the left leg. b, Infrared photograph of the same case demonstrating the dilated skin veins in the left as compared with the right leg. Operation confirmed the arteriographic findings of two arteriovenous fistulas between the femoral artery and vein in Hunter's canal.

of leg to be involved. In the past because of the numerous clinical manifestations these different degrees were not recognized as arising from a single cause. Numerous names were applied, such as phlebarteriectasis, Parkes Weber syndrome, etc., and it is to Lewis and Horton that credit should be given for a clear definition of the underlying pathology and its clinical recognition.

The diagnosis of leg enlargement due to congenital arteriovenous fistula should not present any difficulties if the condition is kept in mind. The salient features on examination are: the leg is definitely but not greatly enlarged and is elongated if the fistulas have shown evidence of their presence before closure of the epiphyseal lines.

This elongation if at all marked will give a lifting of the pelvis on that side and a compensatory scoliosis. There is always an increased prominence of the superficial veins in the involved leg which may progress to the point of showing marked varicosities, and the common varicose vein complications of pigmentation, eczema, and ulceration of the lower leg.

Figure 9 shows an early stage of the condition with the increased superficial veins well demonstrated by infrared photography. This case has been described in a previous commu-

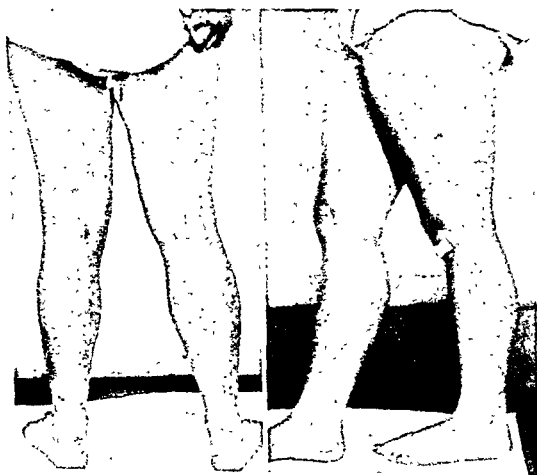


Fig. 10. A case of pseudohypertrophic muscular dystrophy involving the right calf in a girl aged 14 years. The condition did not involve any other muscle groups.



Fig. 11. The right lower leg of a patient showing plexiform neurofibromatosis showing the characteristic greater involvement about the ankle region. This case showed generalized signs of neurofibromatosis.

nication (6). A constant finding is a uniform increase in warmth of the extremity being 1 to 3 degrees C. more than the normal leg. The arterial pulsation in the vessels of the feet is either diminished or absent. A clinical test which is occasionally present is that known as Bragman's sign; that is, occlusion of the artery proximal to the fistula gives a sudden decrease in the pulse rate of 10 to 15 beats per minute. This is more commonly found in the acquired arteriovenous fistulas, and the same can be said for cardiac hypertrophy and failure which follow a well developed arteriovenous communication. These findings will give a tentative diagnosis of the condition and confirmation can be obtained by two further procedures. Arteriography carried out by means of thorotrast or preferably supersaturated diodrast solution will demonstrate the fistulous connections. Examination of the oxygen content of the returning venous blood

central to the fistulas will give much higher values than in normal venous blood, indicating a direct arteriovenous shunt.

#### MISCELLANEOUS

Two separate causes of leg enlargement will be discussed in this group: pseudohypertrophic muscular dystrophy and neurofibromatosis. The former is one variety of the myopathies and should be included in the present discussion because of the frequent commencement of the disease in the muscles of the calf. The history is usually familial and the onset is noticed between the ages of 3 and 15 years. The first symptom if the leg is involved is enlargement of the calf muscles. The condition tends to progress and, in the later stages, if the shoulder and spine muscles are involved there should be little difficulty in diagnosis. The main symptom is a weakness and difficulty in gait giving a marked limp because of increasing incompetence of the involved musculature.

Examination of an early case demonstrates symmetrical enlargement of the calf muscles. The remainder of the leg appears perfectly normal. There are none of the signs such as are present in lymphatic blockage, venous retardation, or arteriovenous fistulas. The clinical impression is that of a diffuse soft tissue mass in the calf area. Soft tissue films show the enlargement in the calf to be beneath the deep fascia. In the case shown in Figure 10, a diagnosis of subfascial lipoma was made; and, at the operation, the findings were solely those of muscle enlargement, which seemed confined almost entirely to the gastrocnemius. Biopsy showed a definite hypertrophy of the fibers and also the deposition of an abnormally large amount of fat in this muscle.

Neurofibromatosis results in leg enlargement from two main varieties, first, from numerous scattered neurofibromas, and second from the plexiform variety. The latter is the more pertinent to our discussion as it causes a diffuse enlargement extending from the foot almost to the knee, usually with folds which droop down overhanging those of the ankle in a hood-like manner. The skin is the typical *café*

*au lait* color and, with the subcutaneous tissue, gives a peculiar putty-like feel. When neurofibromatous overgrowth involves an extremity, associated disturbances in the bones may occur. There may be a mild to massive increase in length and thickness of the long bones together with irregularity in outline which may be of such a degree as to give tumorlike projections and cystic cavities which, however, are found to consist of neurofibromatous tissue. In a recent case of plexiform neurofibromatous enlargement of the lower leg (Fig. 11), a plastic procedure was carried out, and the subcutaneous tissue was found to be extremely vascular and grossly to have the usual appearance of firm whitish jelly. The diagnosis in this group of enlarged legs is obvious because there is invariably associated with it a more or less generalized neurofibromatosis.

#### SUMMARY

1. This presentation is an attempt to organize the scattered information on the subject of the unilateral, chronic, enlarged leg so as to present a guide in its diagnosis. The subject of treatment has been excluded.
2. Six main groups are described, each different from the standpoint of etiology, they are congenital hypertrophy, lymphatic stasis and obstruction, both congenital and acquired, developmental venous retardation; mixed lymphatic and venous partial obstruction; congenital arteriovenous fistulas, and miscellaneous.
3. Group three, that of developmental venous retardation, is presented, as far as can be discovered, for the first time and a case history is given in detail.

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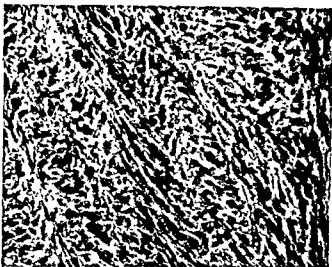


Fig. 4 Sudan stain frozen section revealing characteristic fat droplets in cell protoplasm and lying free in the interstitial tissue  $\times 340$ . (Photography by Clarence B. Mitchell)

*Theca Cell Tumors (Thecoma) — Arthur H. Curtis.*

## THECA CELL TUMORS (THECOMA)

ARTHUR H. CURTIS, M.D., F.A.C.S., Chicago, Illinois

**T**HESE tumors, first described by Moretti and Arrigoni (1927) as fibroma thecocellulare xanthomatodes ovarii, and by Loeffler and Priesel (1932 and 1934) as theca cell tumors of the ovary, are so closely related to granulosa cell tumors that many consider them a variety of the latter. Only 33 cases of theca cell tumor, aside from the one herewith described, have been recorded in the literature; yet there is every reason to believe that these growths, although uncommon, are much less rare than this figure would indicate.

Theca cell tumors are characteristically firm, fibroma-like, nodular, solid or partially cystic, unilateral growths. The tumors are usually not larger than an egg but sometimes attain the size of a small melon. The fundamental characteristic is a connective tissue derivation with a high lipid content. These solid neoplasms arise in the ovary, develop large nodules, and encroach upon and replace the normal tissue.

On gross section, the cut surface is seen to be composed of bands and whorls of fibrous tissue which may be uniformly yellow or there may be yellow islands or streaks of yellowish color. Cysts, an inconstant feature, may have a hemorrhagic content and are commonly the result of necrosis.

Under the microscope the grossly yellow tumor is found to consist of firmly constructed bands of stroma cells varied from spindle-shape to epithelioid form, also a varying proportion of polygonal cells. The stroma cell nuclei are relatively rich in chromatin, uniform in size, and very numerous. The stroma is usually a basket weave with intercellular fibrils surrounding and intermingling with islands of more or less polygonal cells, the latter really an integral part of the growth together with the stroma, although apparently enmeshed in it. Although the spindle cells

usually comprise the major portion of the tumor structure, the nests or large areas of polygonal cells with deeply staining nuclei are a frequent and characteristic finding. The latter cells commonly show some evidence of luteinization, some nests of cells, when viewed under high power, simulating the luteinization encountered in the wall of a lutein cyst (Fig. 5) or even suggestive of the structure of a corpus luteum.

One must not be confused over the relationship of the spindle-shaped stroma cells, the polygonal cells, and the luteinized cells. They are part and parcel of the same structure, varied in degree according to the cellular richness of the growth and the degree of luteinization; the richer the cellular growth, the greater the differentiation in an epithelial direction. The identity in derivation of these various types of cells is evidenced by the Mallory stain, and demonstrated still better by a modified Masson stain. The nature of thecoma tumors has been concisely stated by Loeffler and Priesel: "It is immaterial whether the structure is more a spindle-celled fascicular one or the cells are more of an epithelioid form. The ground type is always a cell of connective tissue derivation with high lipid content."

Despite the firm fibrotic character of most of these growths, numerous thin-walled blood vessels are usually found. Poorly staining hyaline areas in the stroma are so commonly present that they are an almost characteristic feature. Even more noteworthy are minute, scattered, unstained spaces both in and between the cells; in frozen sections prepared with sudan stain these are found to contain fat droplets, not only present in the cell protoplasm throughout, but also lying free in the interstitial tissue.

Our case is that of a nulliparous married woman who continued to menstruate regularly and rather freely despite her age of 52 years. Aside from a fixed very hard tender swelling in the region of the left ovary the only other noteworthy item in the history

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Fig 1 Theca cell tumor of ovary. This was a smoothly nodular, very firm tumor. The cut surface revealed a markedly yellow, smooth, fibrotic tumor, surrounded by a crescent of unusually firm ovarian tissue.  $\times 123$ .

was a recently developed adenoma of the thyroid gland.

At operation, November 29, 1938, there were encountered a marked brawny fibrosis of the cellular tissues of the pelvis, scattered adhesions, multiple small fibroids of the uterus, and a somewhat adherent, tumorous, smoothly nodular left ovary.

The left ovary measured 4 by 3 by 3 centimeters (Fig 1). The surface was smoothly nodular, board-like in firmness. The cut surface revealed  $\frac{1}{4}$  of the substance converted into a markedly yellow, smooth, fibrotic tumor, surrounding which was a crescent of unusually firm ovarian tissue. There were no cystic

cavities and no other gross evidence of degeneration or necrosis.

**Histology.** The tumor is mostly encapsulated, but in one broad area the fibrous stroma of the ovary passes over into the tumor tissue without a discernible zone of demarcation. The new-growth is composed of firm strands of spindle cells with a tendency to create a basket weave, with inter-



Fig 2 The tumor is composed of firm strands of spindle cells with a tendency to create a basket weave with intercellular fibrils surrounding and intermingling with clusters of cells having numerous deeply staining nuclei.  $\times 160$ .

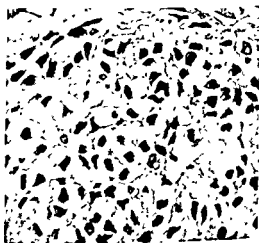


Fig 3 High power photomicrograph of cluster of characteristic polygonal cells with epithelioid tendency.  $\times 335$ .

cellular fibrils surrounding and intermingling with clusters and larger areas of cells having numerous deeply staining nuclei. These cells are polygonal in many areas, in some the cell boundaries are less clearly defined, and in still other regions the clusters of cells show definite evidence of luteinization. Much new-growth of intercellular fibrillar material is strongly in evidence.

In many areas the tumor consists largely of spindle-celled fasciculi, in others the stroma is more epithelioid, with clearly definable transition from the spindle-cell to the epithelioid-cell type. The identity of the elements comprising the tumor is well shown by a modified Masson stain. In sections stained with hematoxylin and eosin are many minute unstained spaces, also displaced individual cell nuclei, leaving clear spaces (fat). Sudan stain of frozen sections reveals innumerable fat droplets in cell protoplasm and lying free in interstitial tissue (Fig. 4, frontispiece).

Chemical analysis of a theca cell tumor shows a moderate amount of lipoid material and a high content of cholestrin. Extraction yields a large amount of estrogen per gram of tumor tissue.

Most of these tumors are in women beyond the menopause. Atypical bleeding in these postmenopausal patients is a characteristic clinical feature. The uterus is enlarged and the endometrium hyperplastic as a result of the elaboration of estrogen by the embryonic tumor cells.

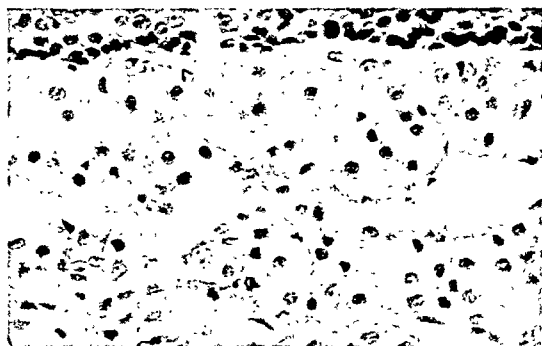


Fig. 5. Section through wall of a large lutein cyst of the ovary with typical luteinization of the theca interna, from a patient with hydatid mole. At the top are seen the granulosa cells which line the cyst cavity. Compare with thecoma cells of Figure 3.  $\times 310$ .

Malignancy may occur but is rare in this kind of tumor in all except the richly cellular type of growth. Unilateral ovariectomy is the treatment of choice.

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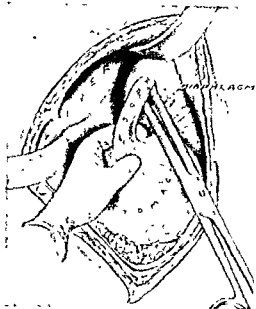


Fig 5 An incision has been made around the esophageal hiatus and the esophagus is being freed by blunt dissection up into the mediastinum.

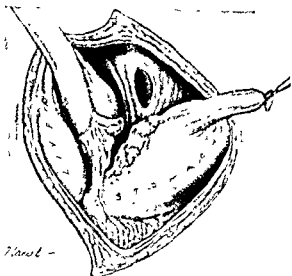


Fig 7 The lesser curvature has been divided so that the stomach may be mobilized

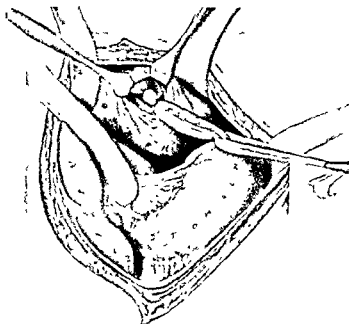


Fig 6 The esophagus has been freed high into the mediastinum and has been doubly ligated with silk

# AN OPERATION FOR THE CURE OF CONGENITAL ATRESIA OF THE ESOPHAGUS

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THE ideal operation for the cure of congenital atresia of the esophagus is one in which a direct attack is made on that portion of the gullet which is deformed and the continuity of the gastrointestinal tract is re-established by an end-to-end anastomosis of the proximal and distal segments of the esophagus. This ideal has been striven for at the Children's Hospital in Boston as reported by Lanman by means of an extrapleural approach through the posterior mediastinum with the result that all of the patients operated upon succumbed, although 1 patient in a total of 5 survived for 8 days and 1 for 9. The remainder were apparently unable to withstand the operative procedure. Probably the next operation in the order of desirability would be one in which the deformed portion of the esophagus is attacked directly either transpleurally or extrapleurally, but in which no attempt is made to re-establish the continuity of the esophagus. The ends of one or both segments of the esophagus are brought out and later continuity is established by reconstructive operations. The Boston Children's Hospital group reported 12 such operations with 100 per cent mortality, and Richter in 1913 reported 2 cases in which, by a transpleural approach, the fistula between esophagus and trachea was ligated, both of which terminated fatally. It would seem to us from these reports, which are the only ones we have found, that the mortality resulting from operations in which the deformed portion of the esophagus is attacked directly is too high to justify their use. We have had no experience with this type of operation and our opinion is based entirely on what has been learned from the work of other surgeons.

In view of the high mortality which results from a direct attack on the deformed portion

of the esophagus, several different operations have been advocated. These operations do not disturb the communication between trachea and esophagus, but attempt to form a new channel whereby food can pass from the proximal segment of the esophagus to the stomach around the fistula mentioned. In the light of our present knowledge it would seem that this type of operation is the most likely to succeed, since the operation can be done in several stages, no one of which is too shocking and, since if leakage occurs, no fatal effects follow. Such an operation should fulfill the following requisites: (a) The blind proximal segment of the esophagus must be drained to the outside. (This is essential for it is the overflow of secretions from this pouch which is responsible for death from pneumonia in nearly all of these patients.) (b) The passage of stomach contents through the lower segment of the esophagus which communicates with the trachea must be prevented, but a long blind pouch of esophagus communicating with the trachea must not remain; otherwise, the secretions from the pouch of esophagus will spill over into the bronchial tree and cause fatal pneumonia. (c) A satisfactorily functioning gastrostomy must be made through which food can be given, but only after the passageway between the distal segment of the esophagus and trachea has been closed. (d) The stomas of the upper segment of the esophagus and the stomach must be as close together as possible to facilitate the later joining of those two stomas by a skin tube.

It does not appear to us that the operations which have been advocated fulfill all of these requirements, nor does the procedure which is advocated in this paper do so completely, but it appears to come closest to such fulfillment. The objections to the operation proposed by Gage are that it leaves a long pouch of the distal esophageal segment still in communication with the trachea and that it leaves the

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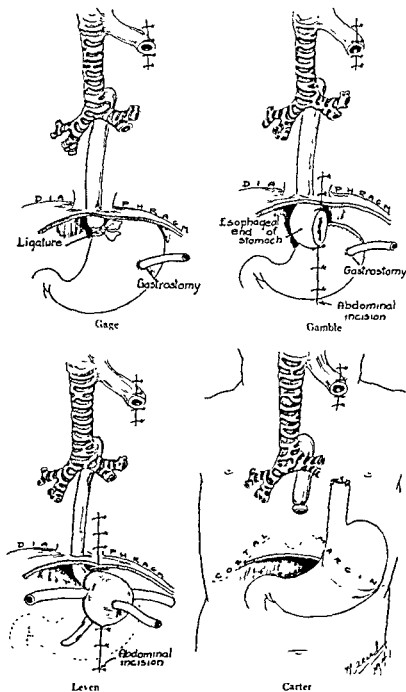


Fig 1. Diagrammatic drawings of the operations by which the tracheoesophageal fistula is undisturbed but the flow of stomach content through it is prevented, and in which it is planned to create a new channel for the passage of food from the mouth to the stomach.

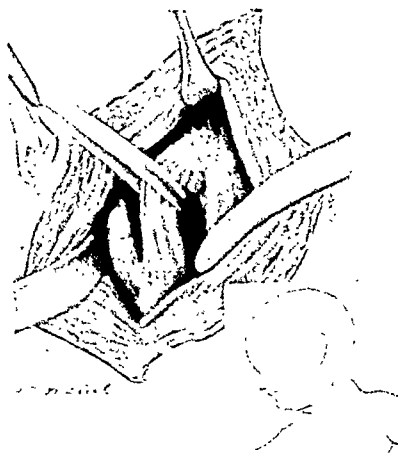


Fig. 2

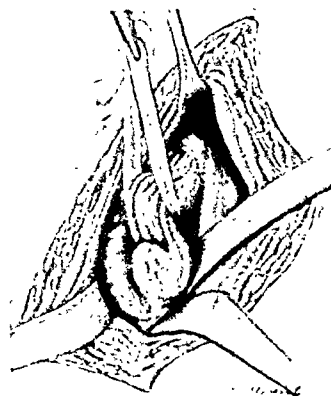


Fig. 3

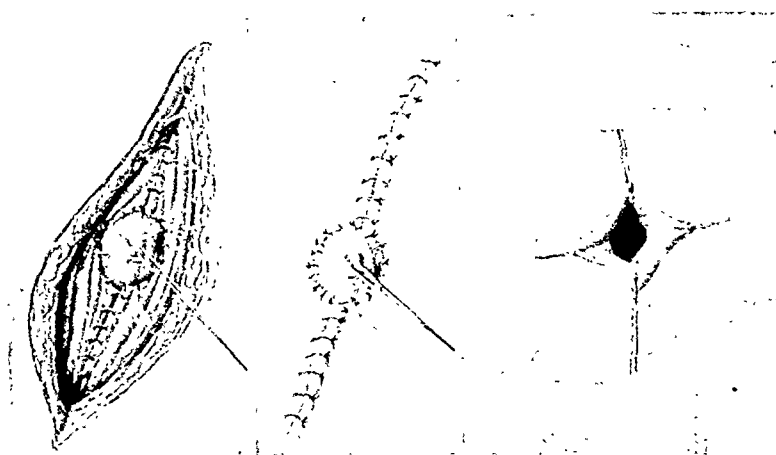


Fig. 4

Fig. 2. An incision has been made along the anterior border of the left sternomastoid muscle. The proximal segment of the esophagus has been freed and a tape has been passed around it.

Fig. 3. The proximal segment of the esophagus has been freed by blunt dissection and pulled up out of the thorax.

Fig. 4. The edges of the muscles and of the skin have been sewed to the esophageal stump, the protruding end of which has been surrounded with strips of collodion gauze. The esophageal stump has been opened and held with 4 traction sutures which have been imbedded in the collodion.

stoma of the proximal end of the esophagus far distant from that of the stomach (Fig. 1). Gamble's ingenious operation (Fig. 1) provides for drainage to the outside of the lower segment of the gullet which is in communication with the trachea but sacrifices one-fourth of the stomach to do so and the gastrostomy is separated from the esophageal stoma by a considerable distance. Also, the

position of the stoma of the distal esophageal segment would interfere considerably with the anastomosis of a skin tube with the gastrostomy. A further objection is said by Lanman to be the respiratory difficulty resulting from the direct communication of the fistula into the trachea with the outside by way of the exteriorized lower esophageal segment. Leven's operation (Fig. 1) is open to much the

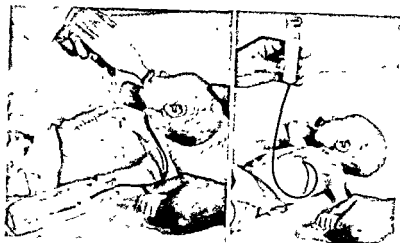


Fig 9

same objections as Gamble's and, in addition, the danger of pressure slough by the tube which is placed beneath the exteriorized esophagus and cardiac end of the stomach would seem very real.

In our experience, 6 cases, the most immediate danger to which infants with congenital

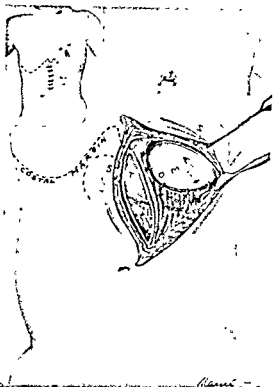


Fig 8

Fig 8 The skin along the left side of the rectus incision has been undermined to above the costal border and retracted. The stomach with the attached portion of the esophagus has been brought out of the abdomen through an incision just below the costal margin and placed in a subcutaneous tunnel terminating at the level of the nipple.

Fig 9, left The feeding taken by mouth is collected in

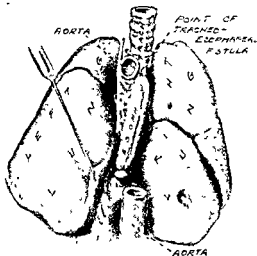


Fig 10

a bottle from upper esophageal stoma, and, right, is then introduced through lower esophageal stoma into stomach.

Fig 10 A drawing made of the autopsy specimen. The blind esophageal pouch was intact and no sign of leakage from it could be discovered. Both lungs showed extensive pneumonia with a bronchial fistula on the right at site of perforation of a subpleural lung abscess.

atresia of the esophagus are exposed is pneumonia caused by aspiration of the overflowing contents of the upper blind esophageal pouch. An unbelievably large amount of secretions comes from this pouch after its blind end has been exteriorized and opened and one can then understand how readily the infant can either drown itself or develop pneumonitis by aspirating the secretions which *overflow* from this segment. Therefore, the first operation, in our opinion, should be the exteriorization of the upper blind esophageal segment.

Under novocain—1:100—anesthesia an incision is made along the anterior border of the left sternomastoid muscle, the neurovascular bundle is retracted laterally, and the thyroid gland medially to expose the esophagus in the neck. The upper segment of the deformed esophagus is usually found to be much dilated; it is freed and cotton tape is passed around it. By traction on the tape and by blunt dissection, this segment of the esophagus can be freed completely and brought out through the wound in the neck. The segment shortens remarkably after it has been freed, so that it cannot be brought out onto the neck far from the working incision and in some instances it barely reaches the skin of the incision. The neck muscles are sutured around the esophageal segment with interrupted catgut sutures, and the skin is sutured with fine silk. Strips of collodion gauze are built up around the exteriorized esophageal stump, and, when they have become hard, the stump is split and held widely open with 4 traction sutures which are imbedded in the collodion (Figs. 2, 3, and 4).

In from 24 to 48 hours the second stage of the operation is performed. Under abdominal wall block, 1:100 novocain, a high left rectus incision is made up to the costal margin. The large fragile liver is carefully and gently retracted, and the esophageal hiatus is exposed. By downward traction on the stomach, the cardiac end of the stomach and the esophageal hiatus can be well exposed. An incision is made through the peritoneum around the hiatus and by blunt dissection the terminal esophagus is freed and pulled down into the abdomen (Fig. 5, frontispiece). Long narrow retractors are placed on the edges of the rent

in the diaphragm and the dissection of the intrathoracic portion of the esophagus continued as far upward as possible. In 1 case our 1.5 inches of the esophagus were freed. A stout ligature of double medium silk is passed around the esophagus on an aneurysm needle, and the esophagus is ligated as tightly and as high as possible (Fig. 6, frontispiece). A second ligature is placed below the first and the esophagus is divided. The last ligature is left long and by traction on it to the left, the lesser curvature is thrown into relief and is ligated and divided about half way down its extent (Fig. 7, frontispiece). Thus the upper half of the stomach is mobilized. The skin on the upper left side of the rectus incision is now undermined to slightly above the costal margin and retracted. An incision is made through the muscle and peritoneum just below the costal margin and the upper end of the stomach with the attached portion of the esophagus is delivered through this incision (Fig. 8). A short transverse incision is made through the skin of the chest wall at the point to which it is estimated that the esophagus and stomach will reach. A subcutaneous tunnel is now made from this incision to the undermined skin flap at the costal margin. The stomach and esophageal stump are now drawn through this tunnel, and the skin edges of the thoracic wall incision are sutured around the esophageal stump (Fig. 8). The abdominal wound is closed in layers with fine silk. The esophageal stump which acts as a gastrostomy tube is opened after 24 hours.

By this operation access to the stomach is via a portion of esophagus which is advantageous in that no actual gastrostomy operation (Witzel, Frank, Janeway) has to be made, the natural relation between esophagus and cardiac end of the stomach is undisturbed, so that leakage of stomach secretions is prevented by the intact musculature at the cardia, by a sufficient length of esophagus, and by the valve-like action of the costal margin. A great advantage is that the gastric stoma is placed high up on the thoracic wall—fourth rib in this case which has been reported—so that there remains only a short gap to be subsequently bridged by means of a skin tube.

The obvious defect in the operation is the fact that a blind esophageal pouch of varying length is left in communication with the trachea. This criticism can only be answered by the fact that in the 1 case herewith reported, there was no evidence during the post-operative course of any spilling over of secretions into the bronchial tree. The patient did die of pneumonia; but clinically this came on as an upper respiratory infection with red throat and with otitis media 42 days after operation. The ideal site of ligation of the esophagus would be very close to the point of fistula into the trachea, so as to leave remaining only as short a blind pouch as possible. Having had the experience with 1 case I believe that a much higher ligation of the esophagus can be achieved at subsequent attempts.

Before the reported operation was performed it had been decided to place a drain into the esophageal hiatus up to the ligated end of the esophageal stump for fear of leakage at the point of ligation. At the operation, however, the esophagus was so small and the danger of infection with the drain was considered so real that no drain was used. The fate of the ligated end of the esophagus caused much speculation and when the pneumonia and empyema came on 50 days after operation, it was suspected that the esophageal stump had finally leaked. At autopsy, however, the esophageal stump was found to be well closed by the ligature which was in place and as far as could be ascertained the esophagus was firmly embedded in scar tissue. It must be remembered, also, that this patient lived 62 days after operation. If leakage was to occur it should have been evident before the expiration of such a length of time. The danger of leakage from the ligated esophageal stump appears to be the greatest danger from the operation and is the weak spot in this operative procedure. It must be borne in mind, however, that there should be little strain on such a ligature since the esophagus above it carries no food, is empty save for some secretion from its mucosa, and has an outlet into the trachea. All that can be said is that in this 1 case there was no leakage and at the end of 62 days the stump appeared

well healed, and there was no evidence of infection about it.

#### CASE REPORT

A 3-day old male infant was admitted to the Children's Hospital (Case 30597) on October 14, 1940. Soon after birth he was noted to have a great deal of mucus in his throat, and at the first feeding became cyanotic dyspneic, and nearly expired. An attempt was made to feed him by gavage, but the catheter would pass only a short distance down the esophagus. Barium was introduced by his pediatrician through the catheter and it was shown by x ray that the esophagus ended in a blind pouch just within the thorax. He was referred to hospital.

His family history was of no significance save that his mother had a threatened abortion at about 2 months and was kept in bed for 6 weeks.

The baby was vigorous, of good development, and presented no evidence of other congenital defects. Aside from many coarse râles in both lungs his physical examination was negative. He was constantly coughing and sputtering saliva. The x ray films which accompanied him showed that a blind pouch represented the upper portion of the esophagus and that the stomach was distended with air. It was obvious that he had the common type of congenital atresia of the esophagus in which its lower segment communicated with the trachea.

He was given 35 cubic centimeters of citrated blood and 40 cubic centimeters of 5 per cent glucose in normal saline solution intravenously. This was followed by 100 cubic centimeters of 5 per cent glucose in normal saline solution under the skin. The throat was kept free of secretions by aspiration and after being in the hospital 6 hours he was operated upon. Under local anesthesia, 1:100 novocain, the blind upper segment of the esophagus was brought out in the neck, surrounded by collodion gauze, and opened (Figs. 2, 3, 4). Much saliva drained through the opening and the coughing and sputtering ceased.

The next day (October 16, 1940) the procedure described and shown in Figures 5, 6, 7, and 8 was carried out under abdominal wall block, 1:100 novocain. The procedure was well tolerated. He received 40 cubic centimeters of citrated blood after operation and his water balance was kept up by intravenous and subcutaneous injections of 5 per cent glucose in normal saline solution.

On the day following operation a small catheter was inserted into the lower esophageal stoma and 5 cubic centimeters of formula—milk 1 water 3—was introduced through it into the stomach. The amount of fluid introduced into the stomach was steadily increased up to 45 cubic centimeters of formula. Like amounts of water were given as indicated to keep up the necessary fluid balance. The wounds healed well and by the twelfth day both wounds were entirely healed and the esophageal stomas were flush with the skin. The lower stoma,

which communicated with the stomach, showed little irritation around it at any time, but the constant flow of saliva from the upper stoma caused some skin damage, necessitating the frequent painting of the skin with compound tincture of benzoin.

There was a steady gain in weight from 6 pounds, 4 ounces immediately after operation to 7 pounds, 5½ ounces, 46 days later at which time an upper respiratory infection had become severe and finally terminated in pneumonia. After the first 2 weeks the child was bottle fed, a catheter was inserted into the upper stoma and the swallowed milk recovered. This was then introduced through the lower stoma into the stomach (Fig. 9). Several times the two stomas were connected by means of a rubber tube and the food was seen to flow rapidly down the tube into the stomach. It was not unusual for the infant to swallow without leakage in this way 2 ounces of formula in 2 minutes.

The convalescence was very gratifying and uncomplicated for 42 days. During this time there was no cough and no evidence of respiratory distress at any time save once or twice when the upper stoma became plugged by the catheter and there was coughing and sputtering when the feeding was given. Serious consideration was being given to connecting the two stomas by a skin tube when the patient developed an upper respiratory infection as evidenced by nasal discharge and catarrhal otitis media. This condition persisted for a week, at the end of which time a frank pneumonia developed. Within 48 hours an empyema was present and a few hours later a bronchial fistula with tension pneumothorax was evident. A closed thoracotomy was performed, sulfathiazole and blood transfusions were given and the patient was placed in an oxygen tent. He rallied considerably after a day or two and great hopes were had for his recovery. The pneumonia spread to the other lung and he died on December 17, 62 days after the completed operation.

An autopsy was performed. The abdomen was entirely negative. The portions of the stomach and esophagus which had been brought out under the skin of the thorax were intact and looked normal. The esophageal stump which had been brought out in the neck was likewise normal. There was a healing empyema cavity in the right pleural cavity. The right lung was practically entirely involved in a pneumonia process and there was a large opening through the lung tissue which communicated with a bronchus. The left lung was involved in a patchy bronchopneumonia throughout about one-third of its extent. The mediastinum was intact and there was no evidence of infection in it. The lower segment of the esophagus was not found to be dilated, it was empty, and communicated with the trachea as shown in Figure 10. Its blind end was well closed by the black silk ligature and by scar tissue and there was no evidence of leakage from it.

There was little shock connected with the operations which were readily done under

local anesthesia. The lower esophageal stoma which communicated with the stomach functioned well in that there was little leakage and consequently little excoriation of the skin. This was probably due to the intact musculature at the esophagogastric junction and to the valve-like action of the costal margin. Peristaltic waves could be seen in that portion of the stomach which had been placed beneath the skin. There was no sign that the short pouch which was still communicating with the trachea was spilling secretions into the bronchial tree in amounts large enough to give symptoms. There was no leakage from the ligated esophagus 62 days after ligation. The cause of the pneumonia cannot be definitely stated, though the clinical picture was that of an upper respiratory infection progressing to a pneumonia rather than to a pneumonia secondary to aspiration of material from the connecting esophageal pouch.

#### SUMMARY

1. A type of operation for the cure of congenital atresia of the esophagus is described in which the proximal segment of the esophagus is brought out in the neck, the distal segment of the esophagus is ligated in the mediastinum as close to the communication with the trachea as possible, divided, and the portion of the esophagus attached to the stomach is brought out as a "gastrostomy tube."

2. The advantages of the operation described are that (1) an ideal type of gastrostomy is provided by using the lower end of the esophagus as a gastrostomy tube and (2) the distance between the two esophageal stomas is short so that they could be readily joined by a skin tube.

3. In the case reported simple ligation of the esophagus with silk did not result in leakage during the 62 days patient survived.

4. The 1 patient operated upon lived for 62 days and died of pneumonia which did not appear to result as a complication of the operation.

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# A STUDY OF THE PLATELET COUNT AND THE COAGULATION TIME OF PLASMA AND WHOLE BLOOD FOLLOWING OPERATION

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**T**HAT platelets influence coagulation is seemingly established, but whether they are essential to coagulation is still a question. Marked increases or decreases in the number of platelets shorten or lengthen the clotting time, but variations of 200,000 per cubic millimeter more or less, from a presumed normal of about 300,000, appear to make little difference in the coagulation time of the blood in the average, normal individual. The elusive character of blood platelets makes it difficult to define a normal numerical level. So many factors influence the number of blood platelets that it becomes difficult to be sure when a count is definitely normal.

In a very exhaustive review of blood platelets in health and disease, Tocantins calls attention to a number of commonplace factors which sharply alter the numerical level of platelets. Violent exercise, he says, will increase the platelet count from 18 to 180 per cent. Even changes in position from horizontal to vertical or vice versa will increase or decrease the count from 20 to 82 per cent. Furthermore, in the winter the counts in both the arterial and venous blood of man are significantly higher than in the spring, and in the summer there is a further decrease in number. Normal menses is associated with a decrease in platelets from 50 to 75 per cent during the first day of menstruation. A slow return to normal occurs during the remainder of the period.

Studies of blood platelets in postoperative patients have been made, and again variable results have been reported. Hueck and Dawbarn, Earlam, and Evans found a postoperative rise in the platelet count from the

sixth to the tenth day. Allen found no significant or uniform variations in the platelet counts or the coagulation time following operation. Rosenbaum failed to observe thrombocytosis in women following thyroid operations. Olef found a drop in platelets during the first 24 hours following operation and a subsequent rise attaining a maximum at 14 days. From a differential study he determined that the increase in numbers was primarily of the small forms.

In 1936 Leslie and Sanford published a method of quantitative and qualitative estimation of platelets in their own plasma. They not only made direct counts of the platelets, but also studied the clotting time of platelet containing plasma and platelet free plasma. The former they labeled plasma A, the latter plasma B. The object of their method is to reduce to a minimum the breaking down of platelets caused by contact with glass, anticoagulants, and tissue juices.

It seemed worth while to utilize this method not only of counting the platelets but also of determining the coagulation time of platelet containing plasma and platelet free plasma in patients after operation. To this was added a record of the coagulation time of whole blood. This report is based on a study of 52 patients who underwent various major surgical procedures, such as: stomach, colon, and rectum resections, prostatectomies, hysterectomies, breast amputations, herniotomies, appendectomies.

## METHOD

A brief description of the procedure published by Leslie and Sanford and since modified by Sanford follows.

The blood is taken from a vein through a fine needle into an iced and oiled syringe and is immediately transferred to an iced, paraffin

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TABLE I.—AVERAGE COUNTS

Date	Platelet count	Coagulation time in minutes		Whole blood
		Plasma A	Plasma B	
Preoperative.....	275,000	7.5	7.	7.5
1st postoperative day.	260,000	7.1	6.6	7.1
3rd postoperative day.	260,000	7.7	7.	7.6
5th postoperative day.	278,000	7.6	6.9	7.4
7th postoperative day.	292,000	7.6	7.	7.6
10th postoperative day.	301,000	7.6	7.	7.7
14th postoperative day.	289,000	7.6	7.2	7.3

coated, hematocrit tube. (A few drops of whole blood are drawn into a capillary pipette for determination of its coagulation time at room temperature.) The tube is packed in ice in a large centrifuge cup and centrifuged at 2000 revolutions for  $1\frac{1}{2}$  minutes. This will throw down the red and white cells but very few of the platelets. A few drops of the platelet containing serum are drawn up into a capillary pipette and its coagulation time at room temperature is determined. A few crystals of heparin are placed in a watch crystal resting on ice, and to these a few drops of the centrifuged plasma are added. After thorough mixing, this plasma is drawn up into a chilled pipette and introduced into a chilled counting chamber resting on ice. After 15 minutes allowed for settling, the count is made under high power. The balance of the plasma is again packed in ice and centrifuged at high speed for 15 minutes. The coagulation time of this plasma, now platelet free, is determined.

## RESULTS

Fifty-two patients were satisfactorily studied. Estimations were made before operation, and in so far as possible, every day or every

TABLE II.—AVERAGE COUNTS, CHOLECYSTECTOMY, MRS. D., AGED 43

Date	Platelet count	Coagulation time in minutes		Whole blood
		Plasma A	Plasma B	
April 6 preoperative....	260,000	7	9	7
April 9 postoperative...	240,000	7	4	8
April 11 postoperative..	182,000	7	6	7
April 12 postoperative..	234,000	6	4	5
April 13 postoperative..	104,000	9	7	8
April 15 postoperative..	305,000	7	6	7
April 17 postoperative..	269,000	6	6	6
April 19 postoperative..	345,000	7	5	4
April 22 postoperative..	216,000	6	6	lost
April 24 postoperative..	359,000	11	9	11

TABLE III.—AVERAGE COUNTS, GASTRIC RESECTION, MRS. C., AGED 41

Date	Platelet count	Coagulation time in minutes		Whole blood
		Plasma A	Plasma B	
April 16 preoperative. .	354,000	6	6	6
April 16 immediately postoperative. ....	352,000	6	6	8
April 17 postoperative...	310,000	6	5	6
April 18 postoperative...	320,000	6	6	8
April 20 postoperative...	320,000	7	6	7
April 23 postoperative...	428,000	9	9	10
April 25 postoperative...	350,000	7	7	8
April 27 postoperative...	390,000	6	6	7
April 30 postoperative...	268,000	5	5	5

other day following operation until the patient's discharge from the hospital.

The average preoperative platelet count was 275,000 per cubic millimeter (Table I). On the first postoperative day the count fell to 260,000 and remained at that level to the third postoperative day. On the fifth day the count rose to 278,000, on the seventh to 292,000 and on the tenth, to 301,000. By the fourteenth day in 24 patients who remained in the hospital it fell to 289,000.

The average coagulation time of the platelet containing plasma A was constantly practically the same as that of whole blood (Table I). Except for a slight drop on the first postoperative day neither varied much at any time. The reason that the coagulation time of serum and blood in this study was longer than the ordinarily accepted normal found in the laboratory lies in the fact that we dealt with chilled blood.

The average coagulation time of platelet free plasma B was constantly slightly less than that of plasma A. This may be due to the breaking down of the platelets during centrifuging, or may be due simply to the lapse of 15 minutes required for centrifuging.

TABLE IV.—AVERAGE COUNTS, BILATERAL HERNIORRHAPHY, MR. B., AGED 50

Date	Platelet count	Coagulation time in minutes		Whole blood
		Plasma A	Plasma B	
February 18 preoperative...	120,000	8	9	lost
February 19 postoperative.	120,000	9	8	lost
February 20 postoperative.	212,000	8	7	10
February 21 postoperative.	180,000	7	7	10
February 22 postoperative..	150,000	6	6	8
February 23 postoperative..	150,000	10	9	10
February 24 postoperative..	184,000	9	8	8
February 27 postoperative..	272,000	9	9	11
March 4 postoperative.....	120,000	7	9	10

A few patients had platelet counts which constantly ranged from 100,000 to 150,000, while others had persistent counts of 350,000 to 400,000. In a third group the individual counts varied from 150,000 to 400,000, from day to day. There was no discernible relationship between the platelet count and the time of coagulation. A platelet count of 120,000 was apt to be associated with a coagulation time of 5 minutes, and a count of 400,000 with a coagulation time of 10 minutes; the reverse was just as apt to obtain. We tried hard to establish a relationship between the count and the coagulation time but could find none.

One patient in this group developed thrombophlebitis the day after he was operated upon for intestinal obstruction. His platelet count ranged from 100,000 to 200,000, and coagulation time of his blood and serum was near the average of the other patients.

The platelet counts and coagulation times of 3 typical patients are recorded in detail to illustrate the variations from day to day (Tables II, III, and IV). It should be mentioned that the technique was mastered before the study was begun and was unchanged thereafter. Practically all of the studies were made during the forenoons of the late winter and spring months.

# CONCLUSIONS

There is a 6 per cent drop from the preoperative level in the average blood platelet count on the first to third postoperative days. This is followed by a slow rise to 9 per cent above the preoperative level on the tenth day following operation.

The preoperative and the postoperative coagulation time of serum and of whole blood remained practically constant with the exception of a very slight drop on the first postoperative day.

In view of the average minimal variations in platelet count and coagulation time in patients who have undergone major surgical procedures, it seems doubtful whether these factors in themselves are of any significance in the development of postoperative thrombosis or embolism.

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# OXYGEN THERAPY IN SHOCK DUE TO HEMORRHAGE

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**S**HOCK produced by hemorrhage results in an anemic anoxemia due to loss of oxygen carrying hemoglobin and also a stagnant anoxemia due to the fall in blood pressure and a decrease in the volume and rate of blood flow.

Wood, Mason, and Blalock have recently reported their results of experiments upon 5 dogs. Shock following the blood loss of 2 per cent of the body weight by repeated hemorrhage produced a depression of the oxygen content of the arterial and venous blood. The blood pressure fell 55 millimeters of mercury and the hematocrit increased from 45 to 47 volumes per cent. After shock had developed, the inhalation of 100 per cent oxygen for only 15 minutes increased the arterial and venous blood oxygen content and the blood pressure rose 6 millimeters of mercury. The effect of more prolonged oxygen therapy was not reported.

Our work was done to determine if the continuous inhalation of high oxygen concentrations had a prolonged beneficial action, increased the tolerance to a greater volume of blood loss, and increased the duration of life of the animals.

## METHODS

These experiments were done upon 20 normal dogs. The animals were deprived of food and water for 12 hours before they were used. One intravenous injection of sodium pentobarbital (25 mgm. per kilogram of body weight) was sufficient to maintain light anesthesia for the duration of the experiment. The left carotid artery was cannulated and attached to a mercury manometer. The dogs were bled  $\frac{1}{2}$  per cent of their body weight from a cannulated left femoral artery every 15 minutes. When the blood pressure fell below 40 millimeters of mercury, the bleeding was reduced to  $\frac{1}{4}$  per cent of the body weight every 15 minutes. Bleeding was discontinued

when the blood pressure fell below 20 millimeters of mercury. Observations of the blood pressure, pulse, and respiration were made every half hour, and the total volume of blood lost and the length of life of each dog was noted. Capillary tube hematocrit determinations were made every hour upon 1 cubic centimeter samples of oxalated blood drawn from the right femoral vein.

Ten of the control dogs breathed atmospheric air (almost 21 per cent oxygen). The 10 treated dogs inhaled 100 per cent oxygen from a Heidbrink gas machine attached to a tracheal cannula.

## RESULTS

Loss of 2 per cent of the body weight in 1 hour by the control group of 10 dogs (Table I) resulted in an average increased hematocrit reading from 42 to 47 volumes per cent. The blood pressure fell from an initial average of 129 millimeters to 75 millimeters of mercury (fall of 54 mm.). The average pulse rate slowed from 153 to 147 per minute and the respiratory rate increased from 10 to 21 per minute. An average of the 10 dogs treated with 100 per cent oxygen (Table II) shows that following the loss of a similar volume of blood the hematocrit increased from 40 to 44 volumes per cent. The blood pressure fell from 137 millimeters to 102 millimeters of mercury (fall of only 35 mm.). The pulse slowed from 153 to 146 per minute, and the respiration increased from 21 to 37.

A blood loss of 4 per cent of the body weight over a period of 2 hours resulted in an average blood pressure of 35 millimeters in the control dogs and 39 millimeters of mercury in the dogs treated with oxygen. The hematocrit was 45 volumes per cent in both groups of dogs. The pulse and respiration was 154 and 35, respectively, in the control dogs and 139 and 39, respectively, in the treated group.

The group of dogs treated with oxygen tolerated a 15 per cent greater volume of blood loss (4.82 per cent of the body weight)

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TABLE I.—SHOCK PRODUCED BY REPEATED SMALL HEMORRHAGE IN NEMBUTALIZED DOGS BREATHING ATMOSPHERIC OXYGEN

Dog	Normal				Bled 2 per cent body weight in 1 hour				Bled 4 per cent body weight in 2 hours				Total blood volume lost in per cent of body weight	Length of life in hours
	Hemato-crit	Blood pressure	Pulse	Respiration	Hemato-crit	Blood pressure	Pulse	Respiration	Hemato-crit	Blood pressure	Pulse	Respiration		
1	35	120	115	6	35	100	120	22	35	40	140	36	4.0	4.00
2	36	145	154	22	50	22	152	51	60	20	150	60	3.0	2.75
3	36	150	152	20	30	105	148	28	40	60	136	72	6.0	3.50
4	38	100	140	10	51	38	124	24	D				2.4	1.83
5	40	120	125	12	38	60	145	32	30	30	100	40	4.5	2.75
6	41	110	156	12	46	100	100	20	42	30	100	28	5.4	3.25
7	45	150	124	4	52	40	144	10	57	30	116	38	3.1	2.50
8	50	118	160	12	52	90	168	22	43	50	204	16	5.0	2.75
9	52	140	170	6	51	80	172	8	51	40	164	10	4.5	3.25
10	47	180	160	12	47	120	132	22	32	30	180	22	4.0	3.25
Av.	42	229	251	20	47	75	147	21	45	35	154	35	4.10	1.08

than the control dogs (4.19 per cent of the body weight). The average life of the dogs breathing atmospheric air was 3.08 hours and that of the dogs treated with oxygen was 3.60 hours (17 per cent longer).

#### EVALUATION OF RESULTS

The series of 10 dogs in each group was sufficiently large to compensate for the individual variations observed. The average initial hematocrit of the control dogs was 2

volumes per cent higher than the treated dogs. Although this is not a great variation in the 2 groups, the control group which had a higher initial hematocrit value could be expected to tolerate a greater loss of red blood cells by hemorrhage than the treated group of dogs with the lower hematocrit. In spite of this, a blood loss of 2 per cent of the body weight produced a fall in the blood pressure of 54 millimeters of mercury in the control dogs and only 35 millimeters in the dogs

TABLE II.—EFFECT OF INHALATION OF 100 PER CENT OXYGEN UPON SHOCK PRODUCED BY HEMORRHAGE IN NEMBUTALIZED DOGS

Dog	Normal				Bled 2 per cent body weight in 1 hour				Bled 4 per cent body weight in 2 hours				Total blood volume lost in per cent of body weight	Length of life in hours
	Hemato-crit	Blood pressure	Pulse	Respiration	Hemato-crit	Blood pressure	Pulse	Respiration	Hemato-crit	Blood pressure	Pulse	Respiration		
1	35	120	140	16	35	110	164	28	35	40	144	36	3.5	3.75
2	36	136	160	8	39	80	140	40	41	34	128	56	4.5	3.00
3	38	150	168	16	51	140	150	60	40	50	144	16	5.1	4.33
4	38	140	144	22	40	110	160	16	37	35	154	48	4.7	3.75
5	40	130	160	20	43	90	168	20	44	40	150	35	4.7	3.25
6	40	140	144	10	47	118	144	20	35	30	130	28	5.2	4.08
7	42	120	162	16	48	80	140	35	34	20	110	26	4.0	3.25
8	43	150	160	25	42	100	144	64	41	41	164	68	4.6	3.25
9	46	130	120	68	40	50	85	44	50	40	100	40	4.4	3.75
10	48	150	160	16	37	140	140	40	50	65	118	40	5.5	3.66
Av.	40	137	151	31	44	102	146	37	41	30	119	30	4.89	1.60

treated with oxygen. After a blood loss of 4 per cent of the body weight over a period of 2 hours the blood pressure was 35 millimeters in the control dogs and 39 millimeters in the treated group. This demonstrates that oxygen therapy exerts a prolonged beneficial action upon the blood pressure. Anoxemia deprives the body of the important carotid sinus mechanism for maintaining the blood pressure. Gellhorn and Lambert reported that anoxemia greatly reduced the pressor reflexes of the carotid sinus in narcotized dogs. In addition anoxemia may cause a decreased blood volume by a loss of circulating fluids and protein through the anoxic capillary wall into the tissues. Landis has reported that the anoxic capillary wall of the frog's mesentery failed to retain plasma proteins and the permeability to fluid was increased 3 times normal.

Although theoretically one might expect a decrease in the hematocrit values following hemorrhage, an increased reading was observed in the majority of our dogs. Compensatory contraction of the liver, spleen, and areas of the capillary bed, press stagnant red blood cells into the circulation. This, augmented by loss of circulating fluid and protein through the anoxic capillary wall into the tissues, makes possible an increased, instead of a decreased, hematocrit.

Oxygen therapy in shock increases the oxygen content of the arterial and venous blood and therefore the amount available to the tissues. Our dogs treated with 100 per cent oxygen inhalation accordingly tolerated a 15

per cent greater blood loss and lived 17 per cent longer than the control dogs.

#### CONCLUSIONS

1. Inhalation of 100 per cent oxygen exerted a beneficial action upon shock produced by repeated small hemorrhage in dogs.

2. A blood loss of 2 per cent of the body weight in 10 control dogs produced a fall of 54 millimeters in the average blood pressure as compared to a fall of 35 millimeters of mercury of the 10 dogs treated with oxygen.

3. A blood loss of 4 per cent of the body weight over a period of 2 hours resulted in an average blood pressure of 35 millimeters in the control dogs and 39 millimeters in the treated dogs.

4. Hemorrhage in both groups increased the hematocrit values by 4 and 5 volumes per cent above normal.

5. The treated dogs had a slower pulse and a faster respiration than the control dogs.

6. The dogs treated by 100 per cent oxygen inhalation not only tolerated a 15 per cent greater blood loss (4.82 per cent body weight) than the control dogs (4.19 per cent of body weight) but also lived 17 per cent longer (3.60 hours) than the controls (3.08 hours).

7. Oxygen inhalation is a valuable adjunct in the treatment of shock following hemorrhage.

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# THE UTERINE CONTRACTIONS OF EARLY PREGNANCY AND THEIR RELATION TO THE DURATION OF LABOR

## A Study of 250 Patients Made with the Lóránd Tocograph

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**I**N a recent report (3) we noted certain changes in the uterine contractions which take place during the last 2 months of pregnancy. These included a progressive increase in the strength, duration, and frequency of the contractions, and also an increase in the tension of the uterine wall.

To supplement that study we are now reporting upon uterine activity over a longer period of gestation. Both studies were undertaken in order to learn the character of the contractions which occur *before* labor, on the hypothesis that such knowledge might assist in a better understanding of the activity which takes place *during* labor.

Specifically the present report deals with: (a) the time at which the contractions can first be detected, (b) the influence of advancing pregnancy upon their occurrence, and (c) the relation between their first appearance and the length of labor.

### MATERIALS AND METHODS

The data, collected between December 1939 and September 1940, were supplied by patients drawn from the Maternity Department of the Hospital of the University of Pennsylvania and the Sheltering Arms Home.

Uterine activity was recorded with the two most recent types of tocograph (1, 2), the observations being carried out under the following conditions. The patient rested in her bed for 5 minutes. The tocograph was then placed upon the most prominent part of her abdomen in the midline, where it was held in place by a webbing girdle. The recording period lasted 30 minutes on the average, during which time note was made of any

voluntary movements which might have influenced the tracing.

After the patients were delivered, the records of those who had presented any evidence of cephalopelvic disproportion or who were delivered by cesarean section were eliminated from further consideration. The presence of (a) intermittent contractions, (b) rhythmicity of contractions, and (c) any increase in the tension of the uterine wall was then determined in the tracings of the remaining patients.

The duration of pregnancy at the time that the records were made was computed from the interval of time elapsing before delivery, on the assumption that pregnancy lasts 280 days. Fetal development and menstrual history likewise were taken into consideration.

### RESULTS

A series of 343 tocographic records was secured from 250 patients. The number of tracings showing contractions, rhythmicity, and an increase in tension of the uterine wall, is shown in Table I, arranged according to the duration of pregnancy at the time that they were made. The number of tracings and individuals corresponds for any given period in all tables, i.e., if a patient supplied two or more tracings during any 1 month, only the first one was employed.

### UTERINE ACTIVITY DURING PREGNANCY

The days in pregnancy when fetal movement and uterine activity were first noted among the 343 tracings are as follows: earliest tracing, 110th day of gestation, earliest fetal movement, 130th day; earliest uterine contractions, 166th day; earliest rhythmicity, 166th day; earliest increase in tension, 222nd day.

TABLE I.—UTERINE ACTIVITY DURING PREGNANCY—343 TOCOGRAPHIC TRACINGS BETWEEN 110TH AND 279TH DAYS, INCLUSIVE

Duration of pregnancy	Tocographic records showing						
	Number	Contractions				Increase in tension	
		Present		Rhythmic			
Weeks, inc.		No. o	Per cent —	No. o	Per cent —	No. o	Per cent —
13-16	1						
17-20	6	0	—	0	—	0	—
21-24	12	1	8.3	1	8.3	2	16.7
25-28	38	2	5.3	1	2.6	7	18.4
29-32	19	3	15.8	1	5.3	3	15.8
33-36	44	17	38.6	6	13.6	11	25.0
37-40	223	158	70.9	78	35.0	97	43.5
Totals	343	175	—	87	—	120	—

Note: (a) absence of activity prior to the 21st week, (b) its subsequent progressive increase, (c) its greatest increase about the 32nd week and (d) the lack of 100 per cent activity during the last 4 weeks of gestation.

Contractions were observed in 51 per cent of all tracings taken during pregnancy, an increase in tension in 35 per cent, and rhythmicity in 25 per cent. The incidence of contractions might have been greater had the periods of observation been longer than 30 minutes.

*Contractions.* Intermittent contractions were not recorded until the 166th day of gestation, which was 56 days after the first tracing was made, and 36 days after fetal movement first appeared. Subsequently, the contractions recurred with increasing frequency (Table I). This increase, however, was not uniform. Breaking down the figures in Table I for the 2 months, from the 29th to the 36th week of pregnancy, inclusive, we find the incidence of contractions from week to week as shown in Table II. The first significant increase in activity appeared during the 32nd week of gestation.

Although the incidence of contractions increased as pregnancy advanced, only 70.9 per cent of tracings recorded their presence during the last month, and only 84 per cent during the last week.

*Rhythmicity.* Rhythmicity appeared as early in pregnancy as contractions (Table I), but subsequently was observed less frequently. It increased in frequency also as pregnancy progressed, and like contractions, it increased

TABLE II.—INCIDENCE OF UTERINE CONTRACTIONS FROM 29TH TO 36TH WEEK OF GESTATION, INCLUSIVE

Week of pregnancy	Tracings showing contractions	
	Present No.	Absent No.
29	0	6
30	1	5
31	0	3
32	2	2
33	3	10
34	4	5
35	6	5
36	4	7

Note increase in number of tracings recording contractions beginning at the 32nd week.

at the greatest rate about the 32nd week of gestation. During the last month it appeared in only 35 per cent of tracings, and during the last week in only 60 per cent.

*Increase in tension of the uterine wall.* An appreciable increase in the tension of the uterine wall was first observed on the 222nd day of gestation, which was 56 days after uterine contractions were first noted. It also increased in frequency as pregnancy progressed, showing its greatest increase, like the two other characteristics, about the end of the 32nd week of gestation. During the last month it was present in only 43.5 per cent of tracings and during the last week in only 52.3 per cent.

TABLE III.—EFFECT OF CONTRACTIONS UPON THE DURATION OF LABOR

Duration of pregnancy	Contractions			
	Present		Absent	
	Tracings	Average duration of labor	Tracings	Average duration of labor
Weeks, inc.	No. o	Hours —	No. 1	Hours 8.0 ± 0.0
13-16	0	—	6	19.6 ± 17.5
17-20	0	—	6	19.6 ± 17.5
21-24	1	2.3 ± 0.0	11	19.0 ± 16.3
25-28	2	6.6 ± 0.7	36	12.1 ± 12.0
29-32	3	4.6 ± 2.4	16	15.2 ± 15.1
33-36	17	14.4 ± 13.5	27	12.9 ± 8.6
37-40	158	13.0 ± 9.7	65	11.2 ± 8.9
Totals	181	—	162	—

Note: (a) absence of contractions prior to 21st week, (b) small number of tracings made before the 33rd week of gestation which recorded the presence of contractions, and (c) the shortness of the labors of the individuals concerned.



TABLE IV.—EFFECT OF CONTRACTIONS UPON THE DURATION OF LABOR ACCORDING TO PARITY

Duration of pregnancy	Contractions							
	Present				Absent			
	Primigravidae		Multigravidae		Primigravidae		Multigravidae	
	Number	Labor Hours	Number	Labor Hours	Number	Labor Hours	Number	Labor Hours
Weeks, inclusive 13-16	0	—	0	—	1	8 0 ± 0 0	0	—
17-20	0	—	0	—	3	15 6 ± 10 1	3	15 6 ± 14 4
21-24	0	—	1	1 3 ± 0 0	8	15 4 ± 14 1	3	20 6 ± 31 0
25-28	1	5 0 ± 0 0	1	7 3 ± 0 0	15	10 3 ± 14 6	11	7 0 ± 5 4
29-32	2	3 3 ± 1 8	1	7 3 ± 0 0	11	10 6 ± 16 3	5	5 7 ± 3 3
Totals	3	—	1	—	38	—	32	—
Weighted average	—	4 2 ± 1 1	—	5 6 ± 0 0	—	10 2 ± 15 0	—	8 9 ± 7 4

Average duration of labor of patients traced prior to 33rd week of pregnancy, arranged according to parity. Note short duration of labor, both multigravidae and primigravidae, whose tracings recorded the presence of contractions.

#### UTERINE ACTIVITY IN RELATION TO DURATION OF LABOR

*Effect of contractions.* The relation between the occurrence of intermittent contractions and the duration of labor is summarized in Table III. If pregnancy is viewed as a whole, the weighted average duration of labor of individuals whose tracing showed contractions was the same as for the persons whose tracings showed no contractions. This statement

TABLE V.—DURATION OF LABOR OF PATIENTS STUDIED BEFORE 33RD WEEK OF PREGNANCY ACCORDING TO PARITY

Parity	Individuals		
	Contractions	Number	Average duration of labor
All	Absent	70	Hours 14 4 ± 10 3
	Present	6	4 2 ± 0 6 Difference 0 ± 9 6 Standard error ± 1 3
Primigravidae	Absent	38	10 1 ± 15 0
	Present	3	4 2 ± 1 3 Difference 15 0 ± 13 8 Standard error ± 0 5
Multigravidae	Absent	32	8 0 ± 7 4
	Present	3	5 6 ± 0 0 Difference 3 3 ± 7 4 Standard error ± 1 1

Note that presence of contractions before 33rd week of gestation has resulted in labors significantly shorter than those of patients who did not exhibit contractions. The difference is more than three times the standard error in the combined group and in the primigravida group, and nearly that in the multigravida group.

likewise is true when considering the effect of the occurrence of contractions during the 33rd to the 40th weeks of pregnancy upon the duration of labor.

Seventy-six tracings were secured prior to the 33rd week of pregnancy (Table III). Of these, only 6, or 7.9 per cent, recorded the occurrence of contractions; the latter tracings belonged to individuals whose average duration of labor was only  $4.9 \pm 1.6$  hours, whereas the 70 tracings showing no contractions belonged to women whose average duration of labor was  $14.5 \pm 13.7$  hours. The difference between these two figures is 9.6 hours and its standard error was found to be 3.1 hours, indicating that the difference is statistically significant.

The duration of labor of these patients in relation to their parity is summarized in Table IV, the totals of which table are compared in Table V. It will be noted in the latter table that the presence of contractions early in pregnancy influenced the duration of labor of the primigravidae to an extent which is statistically significant, and that of the multigravidae to practically the same extent. A difference of three times the standard error is considered significant.

*Effect of rhythm and an increase in tension.* The effect of rhythmicity and an increase in tension upon the duration of labor also was

determined. The early appearance of these characteristics had no effect upon the duration of labor.

#### OBSERVATIONS

The present study indicates that uterine contractions were first observed on the 166th day of gestation. This refers to spontaneously arising movements. Prior to this time we have noted contractions which arose as the result of fetal activity, but none that arose spontaneously. It is apparent, therefore, that the uterus does contract prior to the 166th day under stimulation by the fetus, and it is equally likely that it will contract before that time as the result of manual excitation. The fact, however, that we detected fetal activity considerably in advance of any spontaneously arising uterine activity, suggests that in all probability we have recorded some of the earliest uterine movements.

Although spontaneous uterine contractions begin about the 21st week of gestation, it is of interest that this activity shows its greatest increase about the 32nd week. The reason for this is not known. That the sensitivity of the uterus increases markedly at this time is likewise shown by its response to pituitary extract (4). The administration of this drug at weekly intervals throughout pregnancy has shown that the majority of patients exhibit their first responses to it at this time.

The present study centers about the relation between early activity and the duration of labor. It seems apparent that the patient who experiences early activity is more than likely also to have a short labor. Such a sequence would seem to be a logical one. On the other

hand, the patient who does not experience early activity also may have a short labor.

During the last 2 months of pregnancy (Table III), the mere presence of contractions appears to have no influence upon the duration of labor. Studies are in progress, however, for the purpose of determining whether the magnitude, or any other characteristic of the contractions occurring at this time have prognostic value regarding the nature of the labor.

#### SUMMARY AND CONCLUSIONS

1. The uterine contractions of 250 women were recorded between the 110th and 279th day of pregnancy with a Lóránd tocograph.

2. Although fetal movement was detected as early as the 130th day of gestation, no spontaneous uterine contraction was noted until the 166th day.

3. Uterine activity increased progressively during the remainder of pregnancy, its greatest increase in the middle of pregnancy taking place about the 32nd week.

4. Patients experiencing uterine contractions prior to the 33rd week of gestation experienced significantly shorter labors than those who did not have such activity.

5. The presence of uterine contractions after the 32nd week of pregnancy was of no value in predicting the character of the labor.

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# LIVER INSUFFICIENCY IN TOXIC GOITER AND ITS TREATMENT

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**P**REOPERATIVE management of goiter patients has become a fairly standardized regimen embracing the discriminate use of iodine, a diet high in calories and carbohydrates, sedation, and enforced rest. During the past decade these principles have accomplished much toward lowering mortality and morbidity in thyrotoxic patients subjected to surgery. For all but a limited group of severely toxic patients the present day treatment, in the hands of an experienced surgeon, is entirely adequate. There remains, however, the not too occasional bad risk patient who enters the hospital in impending or actual thyroid crisis. Surgeons have learned that deferring surgery in these individuals reduces the incidence of postoperative complications and lowers postoperative mortality. Such judgment on the part of the surgeon improves operative statistics. It may also be a factor in explaining why, in many localities, thyroid crisis is now encountered more frequently before than after surgery.

More often than not these poor risk patients have carried their goiter a long time, have taken iodine over long periods, and have become refractive to its quieting influence at a time when iodine medication would accomplish the greatest benefit. Frequently, such patients are suffering not from so called hyperthyroidism associated with diffuse hyperplasia of the thyroid, but from a failing heart associated with a nodular, degenerated goiter of long standing. In some the situation is complicated by a toxic psychosis. These severely toxic patients invite continued interest in the pathological physiology of toxic goiter. Controlled observations have convinced us that certain specific therapeutic measures can reduce materially the preoperative and postoperative morbidity in extremely toxic goiter patients.

## LIVER DAMAGE IN THYROTOXICOSIS

The damaging effect of thyrotoxicosis on the liver has been appreciated by pathologists for years. Numerous reports on autopsy studies are in accord (3, 8, 30, 35, 41, 43). Both acute and chronic hepatic lesions are recognized, depending on the severity and duration of the thyrotoxic state. Changes ranging from mildly acute degenerative alterations, characterized by fatty metamorphosis and acute necrosis, to subacute toxic atrophy and cirrhosis have been described. The most extensive degenerative changes have been encountered in thyroid crisis, and a few authorities favor the idea that acute hepatic failure is the underlying basis of thyroid crisis (7, 11, 21).

Interpretation of pathological alterations in the liver of a patient subjected to extreme degrees of fever during thyroid crisis must be guarded. How can one decide in retrospect whether the disintegration of hepatic parenchyma produced, or was the result of, hyperpyrexia? Notwithstanding this controversial aspect, the fact remains that typical degenerative hepatic lesions have been found repeatedly in association with toxic goiter in which extreme degrees of fever was not a part of the clinical picture. Using microscopic sections of autopsy material as criteria, one can but speculate on the degree of impaired hepatic function before death. Beaver and Pemberton in an analysis of the hepatic changes in 107 cases of exophthalmic goiter, stated that the hepatic lesions were such that disturbed hepatic function would have been anticipated in 40 per cent of the cases. It seems probable that the functional state of the liver cell must be compromised appreciably long before the stage of outspoken degeneration is reached.

Within the past few years studies of liver function in goiter patients leave no doubt that measurable liver damage, frequently marked, exists in toxic goiter. Using the Quick hippuric

acid test, Bartels found that 130 of 148 cases of hyperthyroidism showed evidence of impaired hepatic function. Boyce and others (18, 27, 37) have also published data on impaired liver function in selected goiter patients; however, we are aware of no comprehensive study pertaining to the incidence of hepatic insufficiency in a significant number of unselected goiter patients. The present report is based on studies begun in November, 1939, on over 200 consecutive patients subjected to thyroidectomy.

#### LIVER FUNCTION TESTS

The ideal liver function test has not been discovered. This is so for several reasons. In the first place the liver possesses multifold functions and no single test could be expected to reveal the status of the organ as a whole. It is the only organ the removal of which causes unexplainable death. Second, the liver is a large organ possessing a tremendous factor of safety and ability to regenerate, facts which demand significant damage before a state of measurable hepatic insufficiency can be demonstrated. Furthermore, the liver is inaccessible; its rôle in metabolism can be investigated in patients only by indirect methods. Nevertheless, there are several liver function tests which are of value, particularly if their use is restricted to serial determinations during the course of disease or treatment. These same tests are of considerably less value when they are used solely for diagnostic purposes.

Various liver function tests are aimed at one of many and varied hepatic functions. Sugar tolerance tests are directed at the function of carbohydrate metabolism. Blood determinations for nonprotein nitrogenous constituents have to do with protein metabolism. The various dye elimination tests measure the ability of the Kupffer cells, as well as the rest of the lymphatic reticulo-endothelial system, to remove foreign substances injected into systemic circulation. The hippuric acid test, adapted by Quick (1933), is concerned with the hepatic functions of synthesis and detoxication.

The ability of the liver to detoxify injurious breakdown products arising in the course of normal metabolism or from infectious or dis-

ease processes is of primary importance. It is of especial interest to the surgeon who must frequently evaluate an ill patient as a surgical risk. Toxic substances are changed in the healthy liver to relatively inert products which are subsequently eliminated in the body excretions. These changes are accomplished by biochemical processes involving either oxidation, reduction, deamination, or conjugation. All are vital processes. When the detoxifying ability of the liver is impaired or overtaxed the body as a whole suffers from the resulting toxemia. One of the most common means of hepatic detoxication is the combination of toxic substances with the aminoacid glycine to form a less toxic compound. Glycine is synthesized by the hepatic cells, but the liver does not store it. Ordinarily there is also an exogenous supply of glycine in the protein of the diet. In the absence of exogenous glycine the liver manufactures this substance at a constant and fixed rate (27, 28). The hippuric acid test measures the ability of the liver to manufacture and combine glycine with ingested benzoic acid, itself nontoxic, to form hippuric acid. The hippuric acid is excreted by the kidneys. The validity of the hippuric acid test in various states of liver damage has been established by a number of investigators (2, 7, 27, 28, 29, 37). The test is simple, inexpensive, does not greatly inconvenience the patient, and can be reduplicated with remarkable accuracy in a given individual. Furthermore, it utilizes a normal mechanism and does not put a strain on a liver that may be damaged. Results of the test are not valid in the presence of (1) a pathological process which interferes with the emptying of the stomach or absorption from the intestine, or (2) advanced kidney disease with impaired urea clearance.

During the past year we have employed this and other liver function tests in over 500 medical and surgical patients with and without liver damage. From these data we have satisfied ourselves not only of the reliability of the hippuric acid test but have found it consistently sensitive to degrees of impaired hepatic function not reflected by certain other liver function tests. The test is carried out essentially as described by Quick (29) with several minor modifications:

TABLE I.—CLINICAL CLASSIFICATION OF GOITERS STUDIED

	No	Total	Per cent
Nodular			
Nontoxic	10		
Toxic	75		
Fetal adenoma	38	123	59.4
Diffuse			
Colloid	14		
Hyperplastic	30		
Recurrent	14	78	37.6
Malignant		2	1.0
Hashimoto struma	4	19	

One hour after a light breakfast of tea and toast the patient empties the bladder. This specimen is discarded. The test solution, consisting of 6 grams of sodium benzoate made up to 1 ounce with peppermint water, is given, followed by one-half glass of water. The drinking of water is discouraged but not prohibited during the next 4 hours. Four hours after the test solution is given the bladder is again emptied. If the patient has voided during the test period this specimen is included with the 4 hour specimen. It is imperative that all urine formed during the 4 hour period be collected and that the bladder be empty at the end of this period.

The 4 hour urine specimen is brought to a volume of 145 cubic centimeters. If the volume of the specimen is less than 145 cubic centimeters it is diluted to the specified volume with tap water. As a rule it is necessary to concentrate the specimen by evaporation on a steam bath. Before heating, several drops of glacial acetic acid are added to the urine.

After evaporation, the urine is cooled to room temperature, the final volume is corrected to 145 cubic centimeters and the specimen is transferred to a 250 cubic centimeter beaker of known weight. Then 5 cubic centimeters of concentrated hydrochloric acid is added and the specimen is stirred vigorously with a glass rod for several minutes to precipitate the hippuric acid completely. The acidity is tested with Congo red indicator paper. If the color does not change from red to blue more concentrated hydrochloric acid is added until this color change is produced.

The beaker is allowed to stand at room temperature for 30 minutes. The precipitate is then stirred and transferred to a moistened filter paper in a Buchner funnel and filtered by suction. The precipitate is washed once with a 20 cubic centimeter portion of cold water and air is allowed to be drawn, by suction through the precipitate for several minutes. The precipitate and filter paper are transferred back to the 250 cubic centimeter beaker and allowed to dry at room temperature 16 to 20 hours. The beaker and its contents are weighed.

Calculation. Weight of beaker and contents minus weight of beaker and paper plus 0.50 grams equals grams of hippuric acid excreted in 4 hours. The value 0.50 grams represents the amount of hippuric acid dissolved in 150 cubic centimeters of acidified urine. The purpose in making the volume to 150

cubic centimeters is to avoid variables which might be introduced by varying too greatly the volume from which the hippuric acid was precipitated.

We have found that 150 patients in whom there was no reason to suspect liver damage excreted from 4.5 to 5.5 grams of hippuric acid in 4 hours following the ingestion of 6 grams of sodium benzoate. We report hippuric acid values in terms of per cent, using 5 grams (average of 150 normal subjects) as 100 per cent. A value of 90 per cent is considered the lower limit of normal.

Having available a reliable means of estimating one clinically important phase of hepatic activity, we have attempted to evaluate, using quantitative data instead of clinical impressions, the efficacy of therapeutic measures directed at improving impaired liver function in goiter patients. Our observations demonstrate a striking physiological relationship between toxic goiter and the liver. The functional state of the liver appears to have a profound influence on postoperative morbidity, is in turn suppressed significantly by postoperative febrile states. Marked elevation of basal metabolic rate is frequently associated with impaired liver function; however, the greatest degrees of hepatic insufficiency were encountered in toxic patients with chronic thyroid disease in whom the basal metabolic rate was normal or only slightly elevated (apathetic hyperthyroidism of Lahey). Toxic psychosis in goiter patients, either before or following surgery, is preceded and accompanied by evidence of hepatic insufficiency. Finally, selection of anesthesia for thyroidectomy is of utmost importance if liver damage is to be minimized as a result of the operative procedure.

#### INCIDENCE OF LIVER INSUFFICIENCY IN THYROTOXICOSIS

This study is based on 207 consecutive, unselected goiter patients subjected to thyroidectomy. In Table I the patients are grouped according to the clinical and laboratory diagnosis. Approximately 60 per cent had nodular goiters, in 38 per cent the thyroid was diffusely enlarged, slightly less than 2 per cent presented Hashimoto struma, and in 2 instances (less than 1 per cent) malignancy was suspected and found.

Upon admission to the hospital 55 per cent of the group as a whole had subnormal liver

TABLE II.—INCIDENCE AND DEGREE OF LIVER INSUFFICIENCY IN GOITER IN 207 CONSECUTIVE CASES

Clinical classification	Per cent of series	Liver function									
		Normal		Impaired							
				Moderate		Marked		Severe		Extreme	
		100 per cent or over	90 to 100 per cent	80 to 90 per cent	70 to 80 per cent	60 to 70 per cent	50 to 60 per cent	40 to 50 per cent	30 to 40 per cent	20 to 30 per cent	10 to 20 per cent
Nodular nontoxic	4.7	80	20								
Toxic	36.2	23	15	29	21	4	8				
Fetal adenoma	18.3	36	21	21	21						
Diffuse colloid	6.8	27	38	7	21	7					
Hyperplastic	24.1	16	4	10	24	20	6	6	4	0	6
Recurrent	6.8	64	0	36							
Malignant	1.0	100									
Hashimoto struma	2.0	0	50	0	0	50					

function as measured by the hippuric acid test. The incidence of liver insufficiency, summarized in Table II according to clinical classification, is noteworthy because it reveals a fundamental finding, namely, that liver insufficiency occurs in *all* types of goiter except a few instances of nontoxic nodular goiter.

*Toxic nodular goiter.* In this group 38 per cent showed normal liver function, approximately 29 per cent had mild liver damage, while in the remaining third hepatic function was diminished significantly. Twelve per cent of the group had marked impairment.

*Fetal adenoma.* Approximately three-fourths of the patients in this group had normal or slightly impaired liver function. In the remaining 26 per cent moderately impaired values were obtained. In the majority of the latter the goiters were found to contain varying degrees of degenerative change.

*Diffuse colloid.* Nearly one-third of the patients in this group showed evidence of significant liver damage. At operation these goiters also presented varying degrees of degenerative change.

*Diffuse hyperplastic goiter.* The most severe liver damage was encountered in this group, over half having liver function under 80 per cent of normal. Forty per cent of the patients with diffuse toxic goiter had seriously im-

paired hepatic function (less than 60 per cent of normal). Three patients entered the hospital in thyroid crisis with liver function between 10 and 20 per cent of normal.

#### LIVER INSUFFICIENCY AND BASAL METABOLIC RATE

Correlation of liver damage in our goiter patients with the clinical history and basal metabolic rate reveals some interesting relationships. Duration and intensity of thyroid dysfunction rather than the type of goiter present seems the deciding factor in impaired liver function. This is especially true of patients with goiters of long duration who have had indeterminate weight loss and history suggesting many remissions and exacerbations of the thyrotoxic state. A high percentage of such patients had normal or slightly elevated basal metabolic rate. When liver function and basal metabolic rate are correlated one is forced to the conclusion that no constant relationship exists. More important, it becomes very evident that the basal metabolic rate can be dangerously misleading if it is used as a guide in evaluating a prospective surgical risk. We encountered extreme degrees of functional liver damage in patients with basal rates of plus 30 or less. The relationship between liver function and basal metabolic rate in 45 patients is

TABLE III—EFFECT OF PREOPERATIVE TREATMENT ON LIVER FUNCTION IN TOXIC GOITER

TREATMENT OF TOXIC GOITER									
Patient No Sex Age	Clinical diagnosis	Admission		Preoperative		Operation	Postoperative		
		Basal metabolic rate	Per cent liver function	Days' treatment	Per cent liver function		Per cent 3 days	Per cent 8 days	Basal meta- bolic rate
A. Routine treatment									
5 F 55	Toxic nodular	+35	81	9	84	Bilateral	74	71	+36
10 F 37	Exophthalmic	+35	53	12	52	Lobectomy	30	77	+6
11 F 38	Toxic nodular	+36	82	7	88	Bilateral	81	77	+5
13 F 56	Fetal adenoma	+46	60	12	74	Lobectomy		60	-16
31 F 27	Exophthalmic	+83	64	9	83	Lobectomy		83	+63
38 F 47	Toxic nodular	+63	60	16	55	Lobectomy	0	65	+30
39 F 53	Toxic nodular	+0	79	4	84	Bilateral			-13
111 F 63	Degenerated colloid	+26	73	6	81	Lobectomy	36		+16
123 F 34	Exophthalmic	+61	60	10	55	Bilateral	Fatal crisis		
137 F 36	Toxic nodular	+43	71	5	91	Bilateral	70		-21
B. Insulin-glucose									
4 F 49	Exophthalmic	+64	62	4	94	Bilateral	66	75	+23
8 F 40	Diffuse toxic	+5	67	7	100	Bilateral		85	0
12 F 37	Diffuse toxic	+40	33	6	90	Bilateral	80	97	+13
40 F 27	Diffuse toxic	+71	62	5	85	Bilateral	80	85	+5
87 F 17	Exophthalmic	†	15	22	100	Bilateral	2		+6
C. Liver extract—bile salts									
52 F 45	Diffuse toxic	+66	72	10	85	Bilateral	65	76	+17
63 F 40	Diffuse toxic	+47	80	4	95	Bilateral	81	93	+12
65 F 41	Nodular toxic	+10	73	5	100	Bilateral		90	
90 F 27	Diffuse toxic	+34	77	5	92	Bilateral	73		+10
92 F 35	Diffuse toxic	+45	96	5	100	Bilateral	84	100	-4
117 F 25	Nodular toxic	+39	61	5	85	Bilateral	79	90	+4
145 F 30	Diffuse toxic	+80	74	8	97	Bilateral			
D "Works"									
38 M 43	Exophthalmic	+43	30	5	79	Bilateral	64	96	
48 F 44	Nodular toxic	+23	76	3	100	Bilateral	98	100	0
88 F 44	Nodular toxic	+58	48	7	70	Lobectomy	54	85	-13
94 M 34	Diffuse toxic	+40	83	8	92	Bilateral	67	96	+3
89 F 72	Diffuse toxic	+22	151	33	80	Lobectomy		58	-10
70 F 45	Diffuse toxic	+12	59	6	95	Bilateral			-7
73 F 49	Diffuse toxic	+70	72	8	92	Lobectomy	83	100	+54
110 M 36	Diffuse toxic	+26	154	19	81	Lobectomy	73		-0
128 F 50	Diffuse toxic	+36	65	11	107	Bilateral	94	100	-7
138 F 47	Diffuse toxic	+37	76	11	97	Bilateral	85		
231 F 37	Diffuse toxic	+24	49	10	73	Lobectomy	63	71	-3
136 M 59	Nodular toxic	+18	48	10	86	Bilateral		85	-4
150 M 58	Diffuse toxic	+61	77	8	100	Bilateral	100		

A. Routine treatment. Complete bed rest, sodium bromide 25 grains t.i.d., luminal if necessary, Lugol solution, 25 drops t.i.d., vitamin B complex (Pabon) 30 grains daily. B. Insulin-glucose. Routine treatment plus insulin, 5 units t.i.d. a.c. 200 grams glucose intravenously with insulin, 20 units daily last 3 days before operation. C. Liver extract—bile salts. Routine treatment plus 45 grains liver extract (Wilson) and 30 grains bilon (Lilly) daily. D. "Works". All measures in A, B, and C plus glycine 6 daily.

\*Extremely stormy postoperative course, see text. †Entered hospital in crisis. ‡Delayed recovery due to lobar pneumonia. §Developed toxic psychosis 5 days after admission. ¶Developed beginning crisis day after admission. Both responded to treatment.

shown graphically in Figure 1. If a direct relationship existed between severity of thyroid dysfunction as reflected by the basal metabolic rate and the degree of liver damage associated with thyrotoxicosis, one would expect moderate degrees of impaired function (70 to 80 per cent of normal) with moderately elevated basal rates (up to plus 40) and greatest liver damage with high basal metabolic rates. This is not the case, otherwise the values on the graph (Fig. 1) would fall within the diagonal lines drawn parallel on the graph. Less than half of the patients show such a relationship. On the other hand, the 9 patients represented in the lower left corner of the graph (20 per cent) show normal or moderately elevated basal rates with marked to extreme impaired liver function. This type of goiter patient requires more than ordinary preparation for surgery.

#### SPECIFIC MEASURES TO IMPROVE LIVER FUNCTION

Having demonstrated the presence of measurable hepatic insufficiency in more than half of goiter patients entering the hospital for surgery, several questions become pertinent. Foremost are: (1) How much does liver function improve under conventional treatment? (2) What is effect of thyroidectomy on liver function? (3) What specific measures promote greatest improvement in liver function?

Serial tests of liver function were made on 132 toxic goiter patients. These were made on admission, after a period of preoperative preparation (3 to 10 days or longer), 2 days after operation, and before dismissal, usually on the eighth day after operation. In the 75 remaining patients tests of liver function were made on admission and again before operation in instances in which the initial test was subnormal. Lack of space prevents the publication of the data on all of these patients. Presentation of averages would show the general trend of results but would conceal many significant individual variations. Likewise, to submit only selected cases would lead to overemphasis in one direction or another. Consequently, we have sought to present typical cases in a manner that represents an unbiased cross-section of the group as a whole.

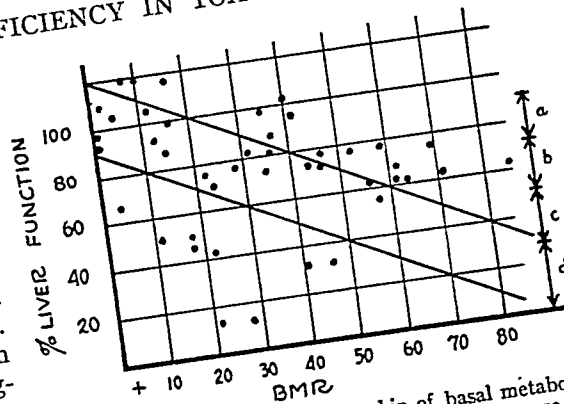


Fig. 1. Graph showing relationship of basal metabolic rate and hepatic insufficiency. a, moderate damage, b, marked damage, c, severe damage, d, extreme damage.

**Control group.** These patients received conventional preoperative treatment including complete bed rest, Lugol's solution, bromides or one of the barbiturates, and a high carbohydrate diet supplying between 3000 and 5000 calories daily. In addition, vitamin B complex (betalin compound, 30 grains daily) was included as part of the routine treatment inasmuch as this had been our practice for more than a year preceding the commencement of the present study.

**"Treated" group.** Together with the treatment outlined, specific measures to improve liver function were instituted. These included (a) intravenous glucose, with and without insulin; (b) insulin; (c) bile salts; (d) liver concentrate; and (e) glycine. These various therapeutic measures were used alone and in different combinations in an attempt to evaluate their individual and collective merits. Table III shows typical results on improved liver function obtained by the various procedures employed. We have concluded that maximum recovery of impaired liver function in toxic goiter is obtained in the shortest period by a regimen including all of the specific procedures listed, i.e. the whole is greater than the sum of its parts. Noteworthy in this respect is the observation that in essentially all instances of toxic goiter the liver damage present is not irreparable. No instance was encountered in which impaired liver function was not greatly improved or normal following specific measures directed at restoring hepatic function. In contrast, a number of patients



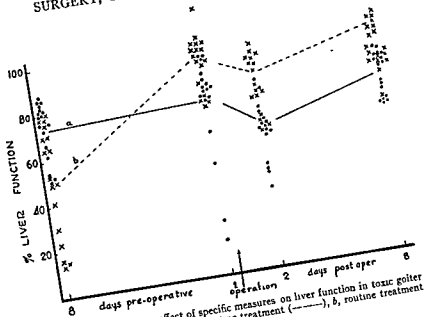


Fig. 2 Graph showing effect of specific measures on liver function in toxic goiter plus specific measures (x---x) and the effect of thyroidectomy a, routine treatment (-----), b, routine treatment

ailed to show comparable improvement on conventional preoperative treatment.

Figure 2 represents a "spot" graph showing the response of patients in the control group compared with patients receiving additional therapeutic measures. Individual values are given to illustrate individual variations. Group averages are shown also. It will be noted that liver function in the control group ranged between 45 and 85 per cent (average 70 per cent) on admission whereas the treated group were far more toxic, showing values varying from 12 to 80 per cent of normal (average 50 per cent). At the end of the preoperative period the general trend in the "treated" group approaches normal in the "control" group. In the conventionally treated series the trend toward improved liver function in some is offset by subjects who showed no response or progressively impaired liver function on routine treatment.

The 2 individuals represented on the graph in Figure 2 with preoperative liver function of 15 and 25 per cent (also in Table III, Nos. 38 and 123) terminated abruptly the desire to secure further data on conventional treatment in extremely toxic goiter patients.

The former, No. 123, a female 24 years of age, had a toxic exophthalmic goiter. On admission liver function was 60 per cent of normal (basal metabolic rate plus 61). Response to routine treatment seemed satisfactory and at the end of 10 days the patient appeared clinically ready for surgery. When the result of the preoperative hippuric acid test was reported the evening before operation it was decided that there had been some error in the performance of the test. A check up in view of subsequent events proved that this was not the case. The standard test solution had been given and retained and the 4-hour urine specimen compared in volume with that obtained when the test was made on admission 10 days previously. A bilateral subtotal thyroidectomy was done. Twelve hours after operation the patient became very restless, and in spite of continuous oxygen and intravenous glucose and iodine, hyperpyrexia to 105 degrees and delirium soon followed. Ice packs reduced body temperature to 102 degrees but the rapid, violent heart pounding persisted and the patient expired 22 hours after operation in typical thyroid crisis. Permission for autopsy was denied.

This was the only postoperative death in this series, and is the first postoperative fatality from any cause in 370 consecutive thyroidectomies.

The other patient (38, Table III) a woman 47 years of age, had a 19 year old toxic nodular goiter

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complicated with auricular fibrillation and moderate congestive heart failure. There had been a weight loss of 25 pounds in the past year, 15 pounds of which were lost during the month prior to admission. After 16 days of routine treatment plus digitalis, a hemithyroidectomy was done. In this instance the results of the preoperative liver function test (25 per cent) were not known until after the patient had been operated upon. Sixteen hours after operation body temperature reached 102.4 degrees where it was controlled with cold sponges. The pulse was rapid, thready, and irregular, and the patient comatose. An extremely stormy postoperative course followed during the next 4 days. Despite full dosage of digitalis and continuous oxygen, cyanosis and dyspnea were prominent. A fasting blood sugar of 356 milligrams per cent was obtained 30 hours after operation. Small infusions of hypertonic glucose and insulin sufficient to maintain normal blood sugar values were given frequently. The 2 day postoperative liver function test was omitted because of the patient's condition; however, clinical jaundice was observed on the evening of the second and on the third postoperative days. Specific measures in addition to glucose and insulin were instituted as soon as nourishment could be taken orally. On the eleventh day after operation, 2 days before dismissal, the hippuric acid test had risen to 63 per cent of normal. Several months later liver function was 90 per cent, and the second stage of the operation was done with essentially no postoperative reaction and an uneventful convalescence.

Five of the patients in the "treated" group (Table III, patients 4, 22, 87, 89, and 119) appeared far more toxic on admission than either of the 2 patients referred to. One entered the hospital in crisis, one developed a beginning crisis 2 days after admission and a third had a toxic psychosis. All responded to specific therapeutic measures and, following surgery, no treatment other than routine was required except in the patient who developed lobar pneumonia on the first postoperative day (Table III, No. 87).

## EFFECT OF THYROIDECTOMY ON LIVER FUNCTION

Nearly all patients subjected to thyroidectomy under local anesthesia for removal of a toxic goiter show a drop of 10 to 20 per cent in liver function on the second postoperative day (Fig. 2). This is transient. By the end of a week, liver function has returned to its preoperative level in nearly all instances. This impairment of liver function as a result of surgery is not due to the preoperative sedation and the local anesthetic (2 ounces of 0.5

per cent novocain). Patients with nontoxic nodular goiter or nontoxic fetal adenoma do not show this drop in liver function following thyroidectomy (Table IV.) Likewise, other patients subjected to surgery other than thyroidectomy (glands or tumors in the neck, benign breast tumors) showed no postoperative impaired liver function following the administration of the same preoperative sedation and novocain given the goiter patients. The damaging effect of thyroidectomy on liver function must therefore be due to some interrelationship between a toxic goiter and the liver. The exact nature of this influence is not known at present.

The comparative data in Table IV is significant. Here it is seen that the average drop in postoperative liver function in a group of patients subjected to hemithyroidectomy was 10 per cent as compared to a drop of 23 per cent in patients undergoing bilateral thyroidectomy. The two stage operation was selected for the former because they were obviously poorer operative risks than the latter. It does not seem that this observed difference in postoperative reaction can be explained satisfactorily on the basis of additional surgical trauma inflicted when both lobes, instead of one, are removed. Only several minutes are required to remove the second lobe after the first is excised. The preoperative medication and quantity of anesthetic are the same for both groups. Equally untenable is the idea that postoperative reaction following thyroidectomy results from thyroid secretion "squeezed" into circulation during the operative manipulation of the gland. Yet it is a widely observed fact that the 2 stage operation may mean the difference between a fatal postoperative reaction and uneventful recovery. Our data on liver function support the following explanation: In toxic goiter an excess of abnormal thyroid secretion is poured into circulation, causing excessive stimulation of metabolic processes, particularly in the liver. It seems likely that in severe, untreated toxic patients the liver has been stimulated to a point where its stored principles are depleted and the majority of hepatic functions are depressed. Corrective therapy, directed at improving specific liver functions, overcomes or

TABLE IV.—EFFECT OF HEMITHYROIDECTOMY AND BILATERAL THYROIDECTOMY ON LIVER FUNCTION

Patient age	Clinical diagnosis	Pre-operative		Liver function		
		Treatment		Days	Per cent pre-operative	Per cent 2 days post-operative

Nontoxic nodular and fetal adenoma (not degenerated) bilateral thyroidectomy						
0 45	Fetal adenoma	Routine		3	84	79
16 24	Nontoxic nodular	Routine		4	92	90
30 46	Nontoxic nodular	Routine		5	100	100
148 31	Nontoxic nodular	Routine		4	100	96
149 40	Fetal adenoma	Routine		3	100	98
		Average			95	92

Toxic nodular and diffuse Bilateral thyroidectomy						
4 48	Exophthalmic	Glucose-insulin		3	94	66
5 37	Toxic nodular	Routine		8	85	65
21 38	Toxic nodular	Routine		10	98	73
52 45	Diffuse toxic	Liver extract, bilron		7	85	65
63 40	Diffuse toxic	Liver extract, bilron		3	95	82
90 37	Diffuse toxic	Liver extract, bilron		3	92	73
91 38	Diffuse toxic	Liver extract, bilron		3	100	84
111 28	Toxic nodular	Routine		8	96	53
117 36	Toxic nodular	Routine		5	92	70
124 34	Exophthalmic	Works		0	92	67
		Average			93	70

Hemithyroidectomy Poor risk patients						
10 37	Exophthalmic	Routine		10	51	51
11 62	Bogen colloid	Routine		6	85	56
21 40	Diffuse toxic	Works		8	92	83
80 74	Diffuse toxic	Works		35	80	78
110 56	Diffuse toxic	Works		10	81	77
131 37	Diffuse toxic	Works		11	73	62
132 57	Diffuse toxic	Works		8	85	70
		Average			78	68

compensates in part the excessive demands made on the liver in thyrotoxicosis. Removal of both lobes of a toxic goiter produces a sudden withdrawal of the stimulating thyroid factor which has been present in excess. In the absence of overstimulation there follows a period of inertia during which the liver per-

forms its functions sluggishly. In contrast, gradual withdrawal of the secretion of a toxic goiter, as in hemithyroidectomy, permits the liver to become readjusted by degrees. Whatever the answer, we do not subscribe to the prevailing theory that surgical trauma alone is the reason why "stage" operations have lowered surgical mortality and postoperative reaction in severely toxic goiters. This question deserves further study.

We have reported elsewhere studies on the effect of different anesthetics on liver function following various surgical procedures (33). Ether and ethylene have been found to result in diminished liver function varying from 20 to 50 per cent. Spinal anesthesia, in the absence of a fall in blood pressure, and local anesthesia (novocain) produce no demonstrable alteration of liver function in general surgical patients. If impaired liver function is to be minimized following thyroidectomy, local anesthesia is by far the anesthetic of choice. In this clinic no other anesthetic has ever been employed for thyroidectomy except in children.

#### RATIONALE OF CORRECTIVE HEPATIC THERAPY

Morphologically two types of cells in the adult liver are responsible for the many and varied hepatic functions. The reticulo-endothelial system (Kupfer cells), lining the hepatic sinusoids, serves to clear hepatic blood of particulate matter—bilirubin, foreign material, bacteria, possibly certain excretory products. Formation of antibodies and antitoxins also is thought to occur in the Kupfer cells. Metabolic, synthetic, detoxicatory, and storage functions are all carried out in the polygonal cells of the hepatic epithelium. In the liver there is no differentiation of special cells to perform special functions. Each hepatic cell is a unit in itself, contributing its share to the multitudinous functions attributed to the liver as an organ.

Much has been written about the liver's enormous functional reserve and its ability to regenerate, two remarkable characteristics of one of the largest and most vital organs. Experimental studies on partially hepatectomized animals, deprived of as much as 75 per cent of their liver without evidence of hepatic insufficiency, have been cited again and again

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to substantiate the view that significant hepatic insufficiency is unlikely unless extensive liver damage has been inflicted. Is such a conclusion warranted? There is an infinite difference between the functional capacity of a liver retaining unimpaired function in a sizeable portion of its substance and one in which every single hepatic cell is compromised. It is well known clinically that diseases of the liver characterized by "patchy" destruction of parenchyma—cirrhosis, metastatic new growths, cyst, or abscess—evidence liver insufficiency late in their course. In contrast, diffuse injury afflicting all cells alike—chloroform, phosphorus or arsenic poisoning, yellow atrophy—are characterized by early hepatic insufficiency.

In toxic goiter we are dealing with a process that affects every cell in the hepatic parenchyma. If one important hepatic function, such as that of detoxication which involves both synthesis and conjugation, is impaired, it seems likely that various other functions performed by the same cell must also be affected, though not necessarily in like degree. We have seen repeatedly abnormal glucose tolerance curves and subnormal prothrombin values in toxic goiter patients with low hippuric acid excretion. All three return to normal after thyroidectomy and can usually be raised to normal before operation by specific corrective measures. The object of specific therapeutic measures is improved liver function, so that the patient is made the best possible operative risk. Each of the measures used in this study has a rational basis and is directed at improving specific liver functions or supplying materials that have been depleted or diminished in an overtaxed liver.

**Glucose.** Glucose offers, perhaps, the most valuable single means of improving liver damage. The ability of glucose to protect against liver damage is well established. It is stored in the liver in the form of glycogen. A liver high in glycogen withstands damaging procedures far better than one depleted of glycogen. Furthermore, glycogen depletion is associated with fatty infiltration of the hepatic cells. Fatty livers are more susceptible to damage than normal livers. The first consideration in treatment then is to load the liver with glycogen. A high carbohydrate diet with intermit-

tent feedings of candy, fruit juices sweetened with dextrose, and fresh fruits, can yield up to 600 grams of glucose daily. This may be augmented in the poor risk patient or one with poor appetite and inadequate caloric intake by parenteral administration of glucose in water. Daily infusions of 1000 cubic centimeters of the 10 per cent solution or from 1 to 2 liters of the isotonic 5 per cent solution are ordinarily well tolerated. For patients with cardiovascular disease 300 to 500 cubic centimeters of 20 per cent glucose given slowly intravenously are of value a day or two preceding operation. If such hypertonic solutions are given rapidly one not only risks overloading the cardiovascular system but may induce a diuresis that could dehydrate the patient if pushed to the limit. This is decidedly undesirable in a prospective candidate for surgery.

**Insulin.** As a result of critical observation, we believe that conservative insulin therapy has a place in the management of severely toxic goiter. Many will disagree with this view. The literature abounds in reports to the effect that insulin, administered to normal laboratory animals, produces a transient increase in liver glycogen at the expense of blood sugar. The resulting hypoglycemia supposedly then accelerates the breakdown of hepatic glycogen to glucose. The end-result is thus diminished rather than increased liver glycogen. We do not doubt that insulin may produce such effects in normal animals and humans. However, a patient with a toxic goiter is not normal. A tendency to postcibal hyperglycemia and glucosuria is widely recognized in toxic goiter. There is good evidence that the removal from the portal blood and storage of glucose in the liver as glycogen is impaired (10, 20, 31). At the same time, increased demand for, and oxidation of, glucose by the tissues is a prominent feature of thyrotoxicosis, and in severe states of the disease the liver may be depleted of glycogen. These features suggest a refractiveness of the thyrotoxic patient to insulin. On the other hand, hypersensitivity to adrenalin is a characteristic of toxic goiter. It is thought that excessive liberation of thyroxin, or a precursor substance arising from a toxic goiter, either stimulates excessive adrenalin secretion or sensitizes

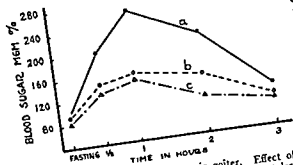


Fig 3 Glucose tolerance in toxic goiter. Effect of bilateral thyroidectomy performed in 12 patients: a, tolerance curve before operation, b, 5 days after operation, c, normal curve.

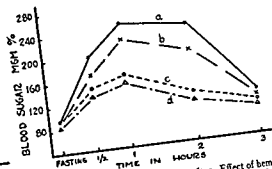


Fig 4 Glucose tolerance in toxic goiter. Effect of hemithyroidectomy in 5 patients: a, before operation, b, after hemithyroidectomy, c, after removal of second lobe several months later, d, normal curve.

sympathetic nerve endings in the liver and tissues so that they respond overactively to normal amounts of adrenalin. Adrenalin induces glycogen depletion by accelerating the breakdown of muscle glycogen to lactic acid and of hepatic glycogen to glucose (9). Insulin has an inhibitory effect on adrenalin glycogenolysis (19). A contributing factor to the hyperglycemia of thyrotoxicosis may be increased hepatic formation of glucose from non-carbohydrate sources (gluconeogenesis). Insulin depresses gluconeogenesis.

While the thyrotoxic patient may not have an absolute deficiency of insulin, at least following the ingestion of carbohydrate there is for several hours a *relative* insulin deficiency. This is well demonstrated in the glucose tolerance curves shown in Figure 3. In these observations blood sugar specimens were obtained in the fasting state and at 1/2, 1, 2, and 3 hours following the ingestion of 1.75 grams of dextrose per kilogram of body weight. Capillary (arterial) blood was used to eliminate the factor of glucose utilization in the tissues. With this technique the maximum height of blood sugar rise, reached at the end of 1 hour, does not normally exceed 160 milligrams per cent. In a few of these patients glucose tolerance curves were obtained following the intravenous injection of the same quantity of dextrose given orally. Two hours were required for the injection. In general, the same type of glucose tolerance curve as that following the oral test was obtained, i.e. an abnormally high

peak maintained over a prolonged period. This indicates that the observed high blood sugar values obtained at 1/2, 1, and 2 hours (Figs. 3 and 4) are not due to accelerated absorption of glucose from the alimentary tract, a theory held by some investigators (1). All of the patients represented in Figure 3 spilled sugar in the urine in the preoperative test. Removal of the goiter was followed by an immediate return to essentially normal glucose tolerance without glucosuria when the test was repeated 5 days after thyroidectomy (Fig. 3). When only half of the goiter was removed the disturbance in glucose tolerance was ameliorated but not corrected (Fig. 4).

In contrast to the abnormal glucose tolerance observed in toxic goiter, a number of tests on patients with nontoxic nodular goiters or fetal adenomas revealed normal glucose tolerance before operation. Removal of the goiter in these patients produced no effect on postoperative glucose tolerance, a fact confirming Gilligan's findings.

Wilder and Sansum found that normal subjects utilized intravenously administered glucose at a rate of 0.85 grams per kilogram per hour whereas thyrotoxic patients could handle only 0.50 to 0.65 grams per kilogram per hour without glucosuria. We found that 5 toxic goiter patients given 100 grams of glucose intravenously during a 2 hour period spilled from 10 to 20 grams of glucose in the urine. Addition of 20 units of regular insulin to the glucose solution eliminated the glucosuria.

Whether the retained glucose was converted to hepatic or muscle glycogen or was burned in the tissues is immaterial from a practical viewpoint. Presumably it was utilized. Improved liver function in one group of patients was obtained when insulin (5 units) was given by injection 3 times daily before meals. In these patients increased appetite and a larger caloric intake may have played a rôle in the improvement. It should be emphasized that insulin therapy is never used without assurance that a constant supply of glucose is available, either orally or parenterally. A detailed study of the effect of insulin on glucose tolerance in thyrotoxicosis is in progress and will be reported elsewhere.

**Bile salts.** Bile salts are manufactured by the hepatic cells exclusively. Animals deprived of bile by external fistula develop extreme weight loss, frequently show changes in behavior, and develop subcutaneous hemorrhages and bleeding from mucosal surfaces. The bone marrow becomes hyperplastic and the bony cortex decalcified. Frequently chronic duodenal ulcers are found at necropsy. Death occurs within several months. When all of the bile secreted is returned to the intestine of such animals a striking economy toward bile salts is shown. Approximately 90 per cent of the total bile salts are absorbed and retained in the enterohepatic circulation. The remaining 10 per cent is lost, but the liver continues to manufacture bile salts at a rate offsetting that lost each day. Thus a balance is kept, preventing a bile salt deficiency (32).

Experiments on animals or patients with biliary fistulas have shown that the synthesis of bile salts is immediately suppressed by minor degrees of liver damage not demonstrable by the usual liver function tests (6, 15, 22, 23, 36). It seems likely that in the presence of measurable liver damage the manufacture of bile salts must be diminished significantly. Prolonged impaired synthesis could result in a relative bile salt deficiency since the liver would be unable to replace the bile salts normally lost each day. We consider all toxic goiter patients with liver function under 75 per cent of normal in this category.

Bile salts are essential for the maximum digestion and absorption of foodstuffs, includ-

ing the fat soluble vitamins A, D, E, and K as well as the minerals calcium and iron. From a practical point of view other effects worthy of consideration have been described. Administration of cholic acid to fed and fasting animals has been reported to increase liver glycogen significantly in acute experiments (24, 39, 40), however, there is no evidence that feeding normal animals bile salts over prolonged periods results in increased glycogen storage in the liver. On the contrary, Ivy (4) has recently observed that prolonged feeding of oxidized bile salt preparations to dogs and rats was without effect on liver glycogen. Intravenous injection of a purified bile salt derivative (decholin) has been reported to double the flow of arterial blood through the hepatic artery without affecting the rate of flow or pressure in the portal system (34). Orally administered oxidized bile salt preparations (decholin, ketochol, and kebilac) have also been found to increase hepatic arterial blood flow (16). This is an important consideration in regard to oxygenation of the liver cells, inasmuch as approximately three-fourths of the blood reaching the liver is venous blood from the portal vein. Increased arterial blood flow without a corresponding increase in portal flow would bring more oxygen to the hepatic parenchyma.

From results obtained clinically in toxic goiter and other states of hepatic insufficiency, we believe that the administration of bile salts is indicated in the treatment of hepatic insufficiency regardless of its cause. In instances in which oral administration is impractical we have used a purified bile salt derivative, sodium dehydrocholate (decholin), with glucose intravenously with results more striking than when glucose alone was given. Such therapy is of course contraindicated in the presence of obstruction to the common bile duct or acute, widespread degeneration of the hepatic parenchyma.

**Liver principles.** The normal liver stores certain essential substances other than glycogen where they can be withdrawn in times of emergency. Examples are antianemic principles and vitamins, particularly vitamin A and those of the B complex. In a damaged liver the function of storage is diminished and

reserves are limited. The increased metabolic turnover, characteristic of toxic goiter, must be met by increased supply of calories and essential materials lest a deficiency arise. Furthermore, the use of a high carbohydrate diet increases the requirement for certain constituents of the vitamin B complex (thiamin and riboflavin) which are essential to intermediary oxidation of carbohydrate and to oxidative reactions in the cells of all tissues. Some of the symptoms of thyrotoxicosis could be explained on the basis of vitamin B deficiency. There is good experimental evidence that large doses of thyroid extract deplete the liver of vitamin B and, conversely, that vitamin B therapy protects the liver against damage when the same amount of extract is fed (12, 13, 26, 38). It is assumed that the condition which results from excessive thyroid extract feeding to animals and thyrotoxicosis in humans are comparable states. Such an assumption is open to question and cannot be taken too literally.

In addition to administration of vitamin B complex, we have used a concentrate of liver (Wilson) representing 100 grams of fresh liver per gram of extract. This preparation is rich in substances normally stored in the liver, known and unknown, including vitamin B fractions. In addition, liver concentrate contains large amounts of choline, a substance which appears to play a rôle in the mobilization and metabolism of liver fat. Experimental studies are in accord that depletion of liver glycogen is accompanied by deposition of intracellular liver fat. Degenerative changes in the liver cells are always preceded by fatty metamorphosis unless the causative agent is overwhelmingly toxic. Fatty livers of animals can be prevented and cured by the feeding of choline (5, 17, 25), and we have observed patients with liver damage who responded slowly to glucose therapy alone markedly benefited by choline fed in the form of pancreatin or liver extract. Preliminary observations indicate that parenterally administered liver extract may be of comparable value in the treatment of hepatic insufficiency when oral therapy is impractical.

*Glycine* Thyrotoxicosis is characterized by increased breakdown of body protein, a nega-

tive nitrogen balance, excessive destruction of phosphocreatin with creatinuria, and reduced synthesis of glycine by the liver cells. The feeding of glycine aids in sparing body protein, furnishes glycine for re-synthesis of muscle phosphocreatin an important constituent necessary for release of energy in muscular contraction, and makes available a substance that can be used by the liver for conjugation and detoxication.

#### SUMMARY AND CONCLUSIONS

Of 207 consecutive goiter patients subjected to thyroidectomy 113, 55 per cent, showed evidence of hepatic insufficiency as measured by the Quick hippuric acid test. In 34 patients, 17 per cent, hippuric acid excretion was less than 70 per cent of normal, indicating appreciable impairment of liver function. Hepatic insufficiency appeared more related to the duration and intensity of the thyrotoxic state rather than to the type of goiter.

No consistent correlation between impaired liver function and basal metabolic rate was observed. Most extensive impairment of liver function was encountered in patients with goiters of long duration having normal or slightly elevated basal rates, and in thyroid crisis. Thyroid crisis and toxic psychosis were preceded or accompanied by evidence of marked hepatic insufficiency.

Serial determinations of liver function were made on toxic goiter patients during preparation for surgery and following operation. In this manner quantitative data were obtained to evaluate the therapeutic measures used during the preoperative period. The hepatic insufficiency present in toxic goiter is not permanent and can be greatly improved by specific measures directed at specific hepatic functions. The rationale of specific corrective hepatic therapy is discussed. Patients receiving this form of treatment showed greater improvement and were better operative risks than the control group of patients treated only by conventional measures now in general use.

The effect of thyroidectomy on glucose tolerance in toxic goiter was studied. The disturbance of carbohydrate metabolism as reflected by glucose tolerance is restored to essentially normal within 5 days after bilateral

thyroidectomy. Hemithyroidectomy ameliorates but does not correct the diminished glucose tolerance of thyrotoxicosis.

Thyroidectomy in toxic goiter has a damaging effect on liver function. This is not due to preoperative sedation and the local anesthetic used, because a number of nontoxic goiter patients and other surgical patients receiving the same medication failed to show postoperative evidence of liver damage. Local anesthesia is considered the anesthetic of choice for thyroidectomy.

It is believed that postoperative morbidity and mortality in severely toxic goiter can be decreased significantly by the use of specific therapeutic measures directed at improving liver function. We have had only the 1 postoperative death described in the text following 370 consecutive goiter operations. This is a mortality rate of 0.27 per cent.

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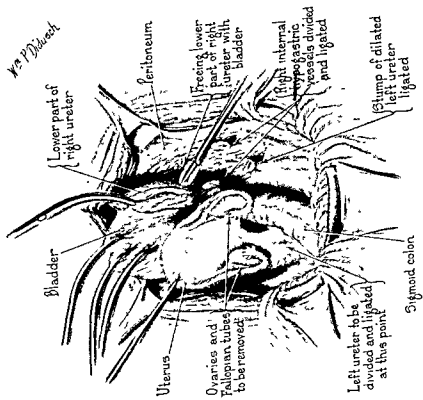


Fig 2 Further steps in operation.

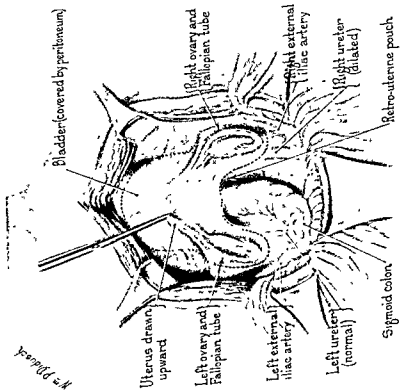


Fig 1 Dotted line indicates extent of peritoneum removed

# TOTAL CYSTECTOMY COMBINED WITH PANHYSTERECTOMY

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**E**XTENSIVE infiltrating carcinoma of the bladder is one of the most discouraging conditions encountered in urology. Radical surgery, although accompanied by relative high mortality, is often the only hope of cure. Only a few extensive infiltrating carcinomas have been reported to be radiosensitive with disappearance of the tumor following adequate deep x-ray therapy. Gross disappearance in most cases has been temporary with recurrence of the tumor later. The effect of deep x-ray, radium, and radon in extensive tumors is at best palliative (2, 3, 4) so that there is every justification for radical surgery whenever possible.

It is well known that extensive tumors of the bladder can exist for considerable periods of time, even years, before metastases occur; hence the bladder in some respects is a favorable site for the application of radical surgery. Unfortunately, a considerable majority of these cases are not suitable for surgery. A great many infiltrating carcinomas involve the base of the bladder, including the trigone and ureteral and vesical orifices, thus complicating the surgical problem.

Total removal of the bladder with diversion of the urine is often the sole hope of cure, or at least relief, from distressing symptoms. Diversion of the urinary stream itself may often be the major problem. Transplantation of the ureters into the sigmoid is perhaps the most ideal procedure, but it is accompanied by appreciable immediate and late mortality. When the trigone area is involved, there is often obstruction of the ureteral orifices resulting in various degrees of dilatation of the upper urinary tract. Patients with dilated ureters and impaired kidneys are poor candidates for ureterosigmoidostomy and when such impairment is present nephrostomy or ureterostomy are the remaining possible procedures. Following diversion of the urine by one of these procedures, complete removal of the urinary bladder is a sound and well established procedure. Hinman has recently reviewed the literature on total cystectomy for cancer and, in 254 cases, the mortality was 34.2 per cent. In the 75 cases reported since 1926 there were 19 operative deaths, a mortality of

25.3 per cent. Such a mortality seems high, but it must be recognized that such patients are doomed and in addition many suffer from intolerable bladder symptoms. From his personal experience Hinman reported 6 of 21 patients living and well after total cystectomy for carcinoma.

It is the purpose of this communication to report an operative procedure which proved invaluable to the authors in a recent case. After preliminary diversion of the urine by means of nephrostomy, an attempt was made to remove the entire urinary bladder, according to the usual technique. In so doing it was found that the carcinoma from the base of the bladder had extended locally through the bladder wall and was beginning to involve the cervix and vaginal vault. The usual technique of total cystectomy was then necessarily modified and combined with panhysterectomy.

Mrs. H. V. S., a 48 year old multipara, was admitted to the Urology Service of the University of Virginia Hospital April 1, 1939 with a history of occasional hematuria since her first pregnancy, 28 years previously. One year before admission she had noticed a gradual increase of bladder irritability with a dull pain in her right flank. She came to the hospital, however, because of sudden severe pain in the left flank associated with chills and fever. For 2 months before admission there had been intermittent hematuria and she had lost about 30 pounds.

Examination revealed a pale, anemic woman who showed evidence of weight loss. Abdominal examination revealed a mass below the right costal margin which was thought to be the right kidney. On vaginal examination a distinct area of induration at the base of the bladder could be felt through the anterior wall of the vagina. The uterus was of normal size, in good position, and freely movable. Cystoscopy revealed an extensive, irregular, papillary tumor involving the entire base of the bladder. It completely obscured the trigone and ureteral orifices and extended upward on the posterior wall for a few centimeters. This tumor began just proximal to the vesical orifice and extended about halfway up on each lateral wall. It was impossible to catheterize the ureteral orifices. Intravenous pyelograms revealed no function in the right kidney after an hour and a half. On the left there was considerable dilatation of the ureter and marked hydronephrosis of the upper half of the kidney. The patient was obviously living upon one-half of the left kidney with little or no renal reserve. The blood urea, however, was normal. X-ray films of abdomen and chest revealed no evidence of metastasis. Hemoglobin was 75 per cent and red cell count was 4.6 million. A biopsy specimen from the tumor showed an epidermoid carcinoma which was estimated to be somewhere between grade II and III malignancy. It was obvious that electrofulguration, radon, and deep x-ray therapy

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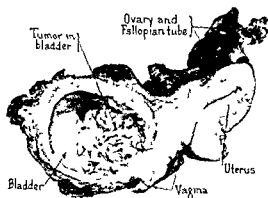


Fig 3 Total specimen removed.

could offer nothing beyond mere palliation for such an extensive tumor.

A left nephrostomy was performed under spinal anesthesia to relieve the bladder symptoms. Following this the patient voided no urine, indicating that the right kidney was completely blocked. The intense bladder symptoms were entirely relieved and the general strength of the patient improved considerably. After much deliberation it was decided to carry out abdominal exploration with the hope that no tumor would be found outside the bladder and a total cystectomy could be performed.

Operation was performed on April 25, 1940. A low, midline, abdominal incision was made from the symphysis to the umbilicus. A careful search was made for evidence of metastases. No palpable lymph nodes were found anywhere in the pelvis or along the aorta. The liver was smooth. A large hydronephrotic, apparently functionless, kidney was present on the right. A large area of induration involving the base of the bladder could be palpated through the anterior bladder wall. The induration did not seem to extend laterally from the confines of the bladder itself. This induration seemed to involve the vaginal vault and cervix and it was obvious that there was no hope of curing the patient unless the cervix, uterus, and upper third of the vagina were removed with the bladder. As this presented the only possibility of cure, the following operative procedure was carried out.

The peritoneum was divided at its reflection from the bladder anteriorly as indicated by Figure 1. The dotted line indicates the extent of peritoneum removed with the operative specimen. The round ligaments were next divided and ligated on both sides. The lateral aspects of the broad ligaments, together with the ovarian arteries, were next divided and ligated. The ureters were then isolated near the brim of the pelvis, divided, and ligated as shown in Figure 2. The distal portions of the ureters, consisting of the last 3 inches, were then dissected up from the floor of the pelvis as shown in Figure 2 and carried forward with the base of the bladder and uterus. Because the ureters were carried forward as shown, the usual procedure of clamping and dividing the uterine arteries was not feasible. It was then decided to ligate the anterior branch of the internal iliac arteries on both sides. These were ligated, together with a moderate amount of surrounding tissue (Fig. 3), followed by division of the ureterosacral ligaments. Ligation of the anterior branch of the internal iliac made division of the ureterosacral ligaments fairly easy. The

uterus was then completely free except for its vaginal and vesical attachments. It was easy to separate the bladder from the symphysis by blunt dissection and to isolate and divide the urethra. The lateral ligaments and blood vessels to the bladder were then clamped, divided, and ligated, so that the uterus and bladder were entirely free except for the vaginal attachments. The vagina was then freed from the rectum posteriorly, following which it was clamped and divided and the total specimen removed in one piece as shown in Figure 3.

A little over 2 hours were required to carry out the operative procedure described. At the end of this time the patient's blood pressure had begun to fall and it was necessary to give her intravenous fluids and a transfusion. It was deemed inadvisable to keep the patient on the operating table longer in order to attempt to reperitonealize the raw area in the pelvis and a sheet rubber dam was placed over the denuded area and brought out the lower angle of the wound. The peritoneal cavity was closed with a continuous suture of plain catgut and the rectus fascia closed with mattress sutures of No. 1 chromic catgut. The vagina was left open and a Penrose drain was inserted from above to the outside.

The patient did remarkably well following this radical procedure and in the subsequent days the pulse rate did not go above 100. There was a slight fever for the first 10 days. For the first few days after operation there was moderate postoperative distention following which there have been no gastrointestinal symptoms whatever. The rubber dam was removed from the lower end of the incision at the end of 1 week and after moderate drainage for a few days, healing promptly occurred. At the end of the second week a thrombophlebitis of the left leg developed with temperature going to 102.6 degrees. As a result of the phlebitis the patient was kept in bed for 3 weeks and at the end of 30 postoperative days she was ready to go home. It was decided to change the nephrostomy tube before discharge. This was unfortunately followed by a chill and a febrile course which delayed her final discharge for 12 additional days. She then left the hospital in good condition, comfortable, and with a hemoglobin the same as on admission.

The patient returned to the hospital 2 months later greatly improved. She had learned to take care of the nephrostomy tube and seemed to be contented. She could go anywhere she wished and had no complaints. The nephrostomy catheter was inadvertently removed and in an effort to insert a larger catheter a false pocket must have been made because catheters could not be reinserted into the kidney. It was necessary to readmit the patient and perform a ureterostomy. The nephrostomy tube was later reinserted so that optimum drainage would take place from her only functioning kidney. This enabled thorough and through irrigation of the kidney to be carried out. She received 12,150 r units of deep x ray therapy to the lower abdomen in the hope that any remaining malignant cells in the perivesical lymphatics might be destroyed. This was given in divided dosages over a period of 53 days by Dr. Vincent W. Archer, roentgenologist to the University Hospital. The patient is now in good general condition and is able to travel and care for her ureterostomy and nephrostomy tubes. She is comfortable, has no complaints, and seems to be satisfied with the results. There have been no symptoms whatever from the nonfunctioning right kidney.

The pathological specimen, Figure 3, consisted of urinary bladder, uterus, tubes, ovaries, a portion of the vagina, the lower several inches of both ureters, broad and round ligaments. It can be seen that the entire floor and trigonal area of the bladder is the site of a raised, irregular, grayish mass, the diameter of which measures roughly 6 by 5 centi-

eters. The ureteral orifices could not be easily identified. The remainder of the bladder wall is normal. Infiltration of the bladder wall by the tumor is readily visible in the photograph and the point at which it was beginning to involve the vesicovaginal septum can be seen. Microscopic section revealed an infiltrating grade III epidermoid carcinoma.

It is obvious that a very radical, extensive procedure was carried out in the foregoing case. We feel that it was justified because any other form of therapy would have been only palliative. Radical surgery was the one chance of possible cure of this patient. It is entirely possible that a cure has not been achieved, and the final result may not be known for years. The patient has at least been entirely relieved of her distressing, almost intolerable, bladder symptoms for the 15 months which have elapsed since operation.

The purpose of reporting this case has been to call attention to the possibility of removing the entire urinary bladder and at the same time combine it with a panhysterectomy. The operation is made feasible by ligation of the anterior branch of the internal iliac artery below the brim of the pelvis. At the time this operation was performed we were unaware that the late Franklin H. Martin (6) first proposed such a procedure for either cancer of the uterus, which had extended to the bladder, or cancer of the bladder, which had extended to the uterus. He believed that it was possible to cure such cases in which all vestiges of malignant tumor could be removed. His technique of removal of the uterus and bladder was somewhat similar to the one which we have used except that he inserted clamps through the vagina for several days to hold the broad ligaments and uterine arteries. The clamps were removed later after obliteration of the vessels had occurred. The operation was carried out by Martin in 1899, at which time he transplanted the ureters into the rectum for diversion of the urine. The patient unfortunately died 4 hours later in shock.

In a review of the literature a similar case was reported by Walton Martin (7) in 1910. He brought the ureters out to the skin margin and stated that at the end of 35 days the patient seemed to be doing well. Antonucci also mentions carrying out a similar operation in 1928. In a very

recent publication Vas Concellos and Da Costa report the use of an identical technique to remove the bladder and internal generative organs. They also stress the ligation of the internal iliac below the origin of the gluteal vessels in order to control bleeding.

The technical success in our case is indicative of the feasibility of carrying out such an extensive operation as total cystectomy combined with panhysterectomy. Such a procedure as we have reported is obviously indicated only in an occasional case. Although our patient is living and well only 15 months, this report will call attention to a valuable operation in the hope that more cases in which it is applicable will be recognized.

#### SUMMARY

1. Extensive carcinoma of the bladder is one of the most distressing and almost surely fatal conditions encountered in urology. Evidence indicates that fulguration, radon, and deep x-ray therapy at the present time offer only palliation.

2. Radical surgery is indicated in extensive carcinoma of the bladder when there is no clinical evidence of extension beyond the bladder wall.

3. A case is presented in which patient suffered from a large epidermoid carcinoma of the bladder infiltrating the base and involving the adjacent portion of the vagina but without evidence of metastasis or extension beyond this area.

4. A surgical technique is shown illustrating the feasibility of removing the entire urinary bladder, together with the uterus, broad and round ligaments, ovaries, tubes, cervix and upper portion of the vagina *en masse*. This procedure, although radical, offers the only hope of cure in such cases as reported here.

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# THE END-RESULTS OF THE TREATMENT OF MALIGNANT TUMORS OF THE PALATE

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THE most common malignant tumors of the palate are squamous cell epitheliomas and adenocarcinomas of the mixed tumor type. In order to determine the results obtained in the treatment of malignant tumors of the palate at the Mayo Clinic, we have reviewed the histories and pathological specimens of 173 cases of malignant tumors in this region which were observed in the years 1907 to 1939, inclusive. During this same period 236 cases of benign tumors of the palate were observed. This makes a total of 409 cases of tumor of the palate. Table I shows the relative incidence of the various benign and malignant tumors of the palate and the sex of the patients.

## ADENOCARCINOMA OF MIXED TUMOR TYPE

Adenocarcinoma, mixed tumor type, presents a characteristic appearance in the palate. It is a hard, rounded tumor with a smooth mucous membrane over the surface, and it is sometimes found on routine examination. The most frequent site of such tumors in the head and neck is the parotid region, but, they may occur in the submaxillary region, floor of mouth, palate, larynx, pharynx, nasopharynx, tongue, upper lip, cheek, and orbit.

They have been given various names by pathologists and show many variations in their histological structure. They have been named fibromyxio-endothelioma, endothelioma, adenocystendothelioma, cylindroma, and chondrocarcinoma, depending upon the predominating type of cell present. Broders expressed the opinion that these tumors are all adenocarcinomas of the mixed tumor type, and this term was used by one of us (New) and Childrey in a report in 1931.

From 1907 to 1939, inclusive, 76 cases of adenocarcinoma, mixed tumor type, of the palate were observed at the Mayo Clinic. Figure 1 shows the various sites of this neoplasm in the head and neck.

When this neoplasm involves the palate, it frequently causes few, if any, symptoms until it becomes rather large. It grows so slowly that the enlargement does not interfere with the function of the pharynx or palate. Mechanical interference

with deglutition and swallowing may be the only symptom if the tumor fills the upper part of the mouth. The patient may notice that the upper denture does not fit, owing to the gradual enlargement of the tumor. Patients may complain of nasal obstruction as a result of extension of the neoplasm into the floor of the nose.

The average age of the patients in the 76 cases at the time of examination was 50 years for males and 42 years for females, the youngest patient was 12 years of age, and the oldest, 80 years. This type of tumor occurs most frequently in the fourth and fifth decades. Table II shows the duration of symptoms. In many of the cases the tumor had been present for many years before it caused the patient to consult a physician. The fact that the tumor had been present for 10 to 20 years in 14 cases is evidence of this.

The tumor may fill the mouth almost completely and the patient may accommodate himself to its presence. The largest tumor was 9 centimeters in diameter, it was lobulated, cystic, and filled the mouth completely. The smallest tumor was 5 millimeters in diameter. Tumors of this type may extend into the nose and antrum or nasopharynx. In 2 cases there was direct intracranial extension through the ethmoid and sphenoid bones.

The average duration of symptoms in the 76 cases was 4.75 years, the shortest duration was 1 month, and the longest, 30 years. In almost half of the cases the tumor was situated at the junction of the hard and soft palate. This might be of some significance since this is the main location for the openings of the ducts of the mucous glands. In 19 of the 76 cases the tumor involved the hard palate, in 16 cases it involved the soft palate. It is rare to see a mixed tumor in the midline (Fig. 2), a tumor was found here in only 4 of the cases.

Usually adenocarcinomas of the mixed tumor type are rather hard, smooth and sessile, and oval in shape (Fig. 3). At times there are soft regions in the tumor, and some tumors are nodular. They are encapsulated to begin with (Figs. 4a and b) and frequently produce a saucer shaped cavity in the bone of the hard palate. Ulceration was present on the surface in 15 of the cases.

TABLE I.—TUMORS OF PALATE: INCIDENCE ACCORDING TO TYPE OF TUMOR AND SEX OF PATIENT

Type of tumor	Cases	Sex	
		Male	Female
Papilloma	115	101	14
Adenoma	8	3	5
Fibroma	16	8	8
Hemangioma	8	6	2
Lymphangioma	3	3	
Lipoma	1		1
Exostosis (torus palatinus)	21	21	50
Foreign body giant cell tumor	1	1	
Total for benign tumors	210	146	64
Squamous cell epithelioma	84	75	9
Adenocarcinoma (mixed tumor type)	70	56	14
Melano epithelioma	3	2	1
Fibrosarcoma	4	1	3
Fibromyxo-sarcoma	1	1	
Myxo-sarcoma	1		1
Chondro-sarcoma	1		1
Lympho-sarcoma	3	2	1
Total for malignant tumors	173	117	56
Total for benign and malignant tumors	383	263	120

The majority of the tumors contain regions of epithelial cells which fade into masses of mucoid material, connective or cartilaginous tissue. It is well known that the epithelial cells of the so called mixed tumors often show a great tendency to polymorphism. This is exemplified by the fact that in these tumors one finds oval cells, round cells, and spindle cells of various sizes. Columnar cells, cuboidal cells, and sometimes squamous cells with intercellular bridges or spines also are found. In the regions of squamous cells one occasionally finds pearly bodies.

The epithelial cells may be arranged in acini, tubules, or alveoli. The tubules often produce a vascular effect. The epithelial cells may also be arranged in solid masses or narrow strands of small, flattened, compact epithelium of basal type, which mingle with stellate, mucous, connective tissue or cartilage cells. Even in cases in which mucous connective tissue and cartilage are absent, the tumors can be recognized as adenocarcinomas of the mixed tumor type. The polymorphism and arrangement of the epithelial cells are the distinctive features. The neoplasm can be

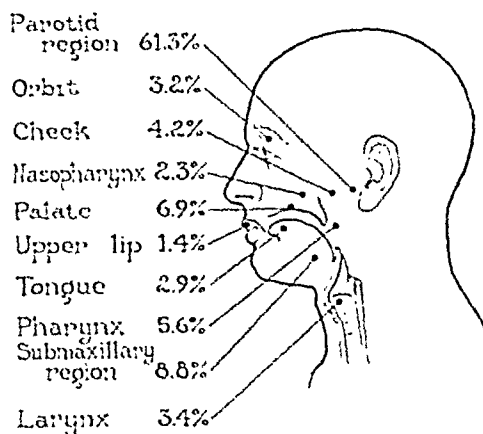


Fig. 1. Incidence of adenocarcinoma, mixed tumor type, of the head and neck according to the site of the lesion.

graded depending upon the appearance of the cell and the amount of mitotic figures present.

There should be little difficulty in diagnosing this type of tumor on the basis of the situation, the long duration, the movable, hard, nodular tumor. Fibromas or fibrosarcomas are about the only tumors that simulate adenocarcinoma of the mixed tumor type. Frozen sections are always prepared at the time of the operation and are examined microscopically.

*Treatment.* Adenocarcinomas of the mixed tumor type are removed surgically when it is at all possible. At times, preliminary ligation of the external carotid is performed, and an incision is made in the palate down to the capsule of the tumor. The tumor is shelled out by blunt or finger dissection. Nitrous oxide-oxygen and ether may be administered intratracheally or pentothal sodium may be given intravenously to produce an-

TABLE II.—DURATION OF SYMPTOMS IN ADENOCARCINOMA OF THE MIXED TUMOR TYPE

Duration of symptoms years	Cases	
	Number	Per cent
Less than 1	17	22.4
1 to 2	10	13.2
2 to 5	20	26.3
5 to 10	5	6.6
10 to 20	14	18.4
20 to 30	2	2.6
Lesion discovered accidentally	6	7.9
Duration not stated	2	2.6
Total	76	100.0



Fig 2, left Adenocarcinoma, mixed tumor type, in midline of palate

Fig 3 Adenocarcinoma, mixed tumor type, of the left side of the palate

esthesia. If the tumor is attached to the periosteum of the bones of the palate, the bone is cauterized with surgical diathermy. If the tumor has extended up into the nose or maxillary sinus, a very wide removal with surgical diathermy is necessary. Radium seeds or needles are used at the time of operation if it is questionable whether the entire tumor has been removed. Perforation of the palate or of the nasal fossa sometimes results. This is later closed with a dental plate. If the tumor is so extensive that complete removal seems impossible, radium seeds or needles are inserted into the neoplasm, sometimes at repeated stages a few months apart. Although this type of tumor is generally not radiosensitive, much

may be accomplished with this type of treatment, particularly in cases in which the tumor recurs.

In all but 1 of the 76 cases the tumor was removed through the mouth. In this case the patient had a large mixed tumor of the palate and maxillary sinus, and resection of the superior maxilla was performed in 1913. He has had several local recurrences since then, but he is well at the present time, 27 years after first operation.

In the 76 cases, the lymph nodes of the neck were not removed unless metastasis was present. Few of these tumors metastasize. In 13 of the cases the lymph nodes of the neck were palpable at the time of the first examination. In 4 of the 13 cases the enlarged lymph nodes were removed.



Fig 4 a, left, Adenocarcinoma of mixed tumor type removed at operation b, Gross appearance of cut section of lesion

TABLE III.—FIVE YEAR AND TEN YEAR SURVIVAL RATES IN CASES OF ADENOCARCINOMA (MIXED TUMOR TYPE) OF THE PALATE

Treatment	Cases*	Patients traced*		Lived 5 or more years after treatment		Patients traced*		Lived 10 or more years after treatment	
		Number	Per cent of traced patients*			Number	Per cent of traced patients*		
Irradiation only (palliative)	7	7	3	43		5	4	1	25
Surgical diathermy and irradiation	14	14	13	93		10	10	9	90
Excision and surgical diathermy (with or without irradiation)	23	22	21	95		19	17	13	76
Excision (only)	9	9	9	100		8	6	6	100
Total	53	52	46	88		42	37	29	78

\*Inquiry as of January 1, 1940. The 5 year survival rate was determined by a study of cases in which the patients were treated 5 or more years before this investigation, that is, in 1934 or earlier. The 10 year survival rate was determined by a study of cases in which the patients were treated in 1929 or earlier.

Microscopic examination of these revealed adenocarcinoma, grade 2 of the mixed tumor type.

In 25 per cent of the 76 cases operation, irradiation, or both had been employed before the patients came to the clinic. In 7 cases in which irradiation had been used alone before the patients came to the clinic, the tumors were so situated and fixed that they were considered inoperable; therefore, irradiation only was used at the clinic.

**Results.** The results of the treatment are shown in Table III. In 9 cases in which there was no recurrence following excision the tumors, which were encapsulated, were shelled out without rupture. In 23 cases in which surgical diathermy was used as well as excision the bone was involved, and it was necessary to destroy the periosteum or part of the bones of the palate or superior maxilla in order to remove the tumor. In the 14 cases in which surgical diathermy and irradiation were used the bone also was involved, and irradiation was used in addition to diathermy.

In the 4 cases in which enlarged lymph nodes in the neck were removed the duration of life was as follows: 1 year in 1 case, 4 years in 1 case, 9 years in 1 case, and in the remaining case the patient is still alive 32 years after operation. The large number of patients who lived 5 and 10 years after treatment tends to prove that most tumors of this type have a low grade of malignancy.

#### SQUAMOUS CELL EPITHELIOMA OF THE PALATE

Primary squamous cell epitheliomas of the palate are infrequent. Because of the fact that in a



Fig. 5. Squamous cell epithelioma, grade 2, of the soft palate.

case of very extensive involvement it is difficult to tell just where the tumor originated, only those cases in which we believe that the tumor started in the palate are included in this series. Tumors that secondarily involve the palate, that is, those that started in the gum, tonsil, pharynx, maxillary sinus, or cheeks, were not included in this group. From 1907 to 1939, inclusive, 84 cases of primary squamous cell epithelioma of the palate were observed at the clinic. During this time approximately 5,000 cases of malignant tumors of the buccal cavity were observed.

Forty per cent of the 84 patients complained of soreness of the mouth. Twelve patients had trouble wearing their dental plates as the plate either did not fit or hurt them. The first symptom in 2 cases was enlarged cervical lymph nodes. One patient complained of bleeding from the mouth. In some cases the growth was found accidentally.

The average age of the patients was 58.2 years, and only 10.7 per cent of the patients were women. The duration of the tumors varied from a few weeks to several years. Sometimes the presence of a thickened leucoplacia may have been noted for years, and then the growth became active and underwent ulceration.

In 50 per cent of the cases the tumor was found in the soft palate, and in 25 cases it was situated in the hard palate alone. In 5 cases the mass was situated in the uvula and the adjacent part of the soft palate; in 2 cases the tumor was situated on the upper surface of the soft palate. In 26, or 30.9 per cent, of the 84 cases the tumor had extended into the adjacent structures, that is, into the nose, nasopharynx, maxillary sinus, and pharynx.

The low grade tumors appear as grayish ulcerated lesions and sometimes are papillary. The more malignant lesions have soft, easily bleeding surfaces. Although the diagnosis in all cases must



TABLE IV.—SQUAMOUS CELL EPITHELIOMA OF THE PALATE: INCIDENCE ACCORDING TO GRADE OF MALIGNANCY

Grade	Cases	
	Number	Per cent
1	11	15.3
2	25	34.7
3	30	41.7
4	6	8.3
Total	72	100.0

be made microscopically by using fresh frozen sections at the time of operation, usually it can be made by the appearance of the lesion (Fig 5).

**Treatment** We believe that removing the local growth with surgical diathermy under anesthesia produced by the intratracheal administration of nitrous oxide-oxygen and ether or by the intravenous use of pentothal sodium offers the best chance of getting rid of the lesion. A large sequestrum usually follows the removal, and the greater part of the soft palate is lost. A dental plate is required to close the opening. Irradiation is administered directly into or over the involved region in cases in which the lesion is active.

Nine patients with palpable glands had gland dissection in addition to the treatment of the local lesion. They all showed involvement microscopically. Of these, 6 returned later to the clinic for examination, and they lived on an average of 5½ years after the initial treatment. Seventeen patients received radium, x-ray, or both. Five did not receive any treatment at the clinic, the lesion being too far advanced, but they had palliative x-ray at home. The grade of the tumor and the results are shown in Tables IV and V.

#### OTHER MALIGNANT TUMORS

The malignant tumors other than the adenocarcinoma and squamous cell epithelioma that were encountered in the 173 cases are listed in Table I. The treatment of these tumors depends upon the activity of the growth. If the tumors are encapsulated, surgical removal is advisable. The use of diathermy and radium depends upon the extent of the lesion. Irradiation is also used externally.

Of the 3 patients who had melanopithelioma and were treated with diathermy and radium, 1 lived 4 years after treatment, and the others, 2 years after treatment. In 1 of them the lesion was inoperable and palliative irradiation was used.

In 4 cases the patients had a fibrosarcoma. In 3 of the cases the tumor was removed surgically and

TABLE V.—RELATION OF FIVE YEAR SURVIVAL RATE TO GRADE OF MALIGNANCY IN CASES OF PRIMARY SQUAMOUS CELL EPITHELIOMA OF THE PALATE

Grade of tumor, on basis of 1 to 4	Cases*	Patients traced*	Lived 5 or more years after treatment	
			Number	Per cent of traced patients
1	5	5	5	100
2	20	16	7	44
3	31	21	8	38
4	5	5		
Not stated†	0	5		
Total	60	51	20	38

\*Inquiry as of January 1, 1940

†In these cases the patients were treated in the years 1910 to 1914, inclusive

the bone destroyed with surgical diathermy. In addition, 1 patient received radium treatment. Of these 3 patients, 1 had no recurrence in 5 years, 1 had none in 10 years, and 1 had none in 20 years, respectively, after the initial treatment. The fourth patient had a very extensive involvement of the palate and a fibrosarcoma, grade 4, involving lymph nodes. Radium was used as a palliative measure, but patient died 1 month later.

The patient who had a fibromyxosarcoma also had extensive involvement of the soft palate and of the lymph nodes in both cervical regions. This patient, a boy, aged 13 years, was treated with radium and x-rays but died 2 years later.

The patient with myxosarcoma of the palate, a girl, aged 7 years, had had difficulty in swallowing for 3 weeks and swelling of lymph nodes of neck for 2 months. She died a month after treatment.

The patient with chondrosarcoma of the palate, a woman, aged 49 years, had had a tumor removed from her palate 10 years before examination at the clinic. The tumor had recurred 4 years prior to her examination at the clinic, and 2 years before her examination a growth had caused bulging of the ala of the nose. At the time of her examination at the clinic, she had a huge hard growth that involved the entire palate and maxillary sinus and caused bulging of the right eye. Palliative roentgen therapy only was employed.

Of the 3 patients with lymphosarcoma, 2 were males and 1 was a female. Their ages were 1 year, 11 years, and 43 years, respectively. They all had palpable lymph nodes at the time of their examination. All received palliative roentgen therapy with some improvement, but they all died within 11 months, apparently of generalized metastasis.

# INTRASPINAL EPIDERMoids, DERMoids, AND DERMAL SINUSES

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INTEREST in rare diseases is aroused first by detailed case reports, but when the series of observations becomes large and diversified, single cases lose their value as curiosities. One is then tempted to combine the mosaic of individual observations into a general pattern and to outline the salient features of the disease entity in question.

For such an undertaking, I have selected the intraspinal epidermoids, dermoids, and dermal sinuses because of an opportunity to observe personally 5 such cases. These, presented below, will bring the total number reported to 56.

First it will be necessary to define what is meant by the terms "epidermoid, dermoid and dermal sinus," because the terminology on this subject is rather confused. For example, frequent reference is made to the "pearly tumor" which merely describes the shiny macroscopic appearance of some epidermoids, or "cholesteatoma" which represents no anatomical entity, but has been used indiscriminately to designate epidermoids, dermoids, certain mesenchymal tumors and chronic inflammatory conditions.

Epidermoids, dermoids, and dermal sinuses are heterotopic formations composed of elements of the skin. They are dysembryonic malformations (hamartomas) rather than true neoplasms, and are referred to in this paper as tumors because of their expanding nature.

Epidermoids are composed of the superficial (epidermal) layers of the skin. Dermoids contain all layers of the skin, epithelial and mesenchymal, and also the accessory cutaneous organs such as sebaceous glands and sweat glands and hair follicles. Dermal sinuses are tubular formations which may have the histological characteristics of epidermoids, dermoids, or both, but which are always in direct connection with the skin. Thus, a pilonidal cyst is a dermal sinus containing hair. In all three of the above conditions named the viable cells form a thin capsule or wall, and the interior consists of cheesy amorphous masses of dead, cornified epithelial cells, and, in dermoids, also of sebaceous matter and hair. Hair-containing tumors have always been classified as der-

moids in this study, even though microscopic examination of the cyst wall showed no cutaneous appendages. As Bostroem pointed out, only a small area of the dermoid cyst wall, the "dermoid villus," may possess hair follicles and other accessory cutaneous structures, whereas the remaining portion is purely epidermal in character.

## ILLUSTRATIVE CASES

### 1. *Epidermoids*

CASE 1. Low back pain syndrome with right sciatic radiculitis. Myelographic evidence of benign intradural tumor at the level of the third lumbar vertebra. Intracranial epidermoid removed. Perfect recovery. R. L., No. 459,514, male, aged 14 years, referred by Dr. W. Towsley, Midland, Michigan, admitted to hospital April 10, 1940.

For 7 months prior to admission, the patient complained of increasingly low back pain with radiation along the posterolateral aspect of the right thigh and calf. The pain was sharp, occasionally shooting in character and was increased or elicited by movements, sneezing, laughing, and straining.

On examination, the patient stood with a protective posture, keeping the right leg flexed in knee and hip and slightly externally rotated. The third and fourth lumbar spinous processes were tender to percussion. Considerable spasm of the erector trunci was present. Extension of the lumbar spine was markedly limited and painful, whereas flexion was only moderately limited. The neurological signs were confined to the right lower extremity, except for Lasègue's sign which was strongly positive on the right and suggestive also on the left. There was flabbiness of right gluteus maximus and hypotonicity in the distal segments of the right lower extremity. Slight paresis was present in the gluteus maximus and hamstring muscles on the right. The right knee reflex and hamstring reflexes were diminished and the ankle reflex was absent on that side. Mild tactile and thermic hypesthesia and hypalgesia were demonstrable in the fifth lumbar and first sacral dermatomes. Sphincter functions were unimpaired.

Spinal puncture, done in the lateral recumbent position, revealed colorless spinal fluid under 155 millimeters pressure of water. There was no manometric block. Cell count was 0; Pandey, positive; total protein, 93 milligrams per cent; goldsol, 001221000; mastic, 221000; Kahn, negative.

Roentgen-ray examination of the lumbar spine showed no bony changes.

Myelography, first done with air, later on repeated with lipiodol, revealed an identical picture in each (Fig. 2a and b). A smooth ovoid, intradural tumor was outlined posterior to the body of the third lumbar vertebra and intervertebral disc below. The tumor did not obstruct the spinal canal completely.

Diagnosis was made of intradural tumor of the cauda equina at the level of the third lumbar vertebra and intervertebral disc below. A benign lesion such as an epidermoid or dermoid was suspected.

From Department of Surgery, Section of Neurosurgery, University of Michigan, Ann Arbor, Michigan.

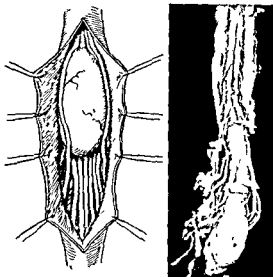


Fig 1. a, left Epidermoid of cauda equina as shown at operation. Case 1 b, Dermoid of lumbosacral portion of the cord. Autopsy specimen, reproduced from Pitot's article

Laminectomy was performed by Dr. M. M. Peet, on April 19, 1940, under avertin-nitrous oxide anesthesia. The posterior laminae of the second, third, and fourth lumbar vertebrae were removed and the dura was opened. A glistening pearly white tumor, the size of a walnut was found lying between the roots of the cauda equina, covered by arachnoid. The tumor looked exactly like a silkworm co-

coon (Fig 2a). It had a thin, avascular capsule and was removed *in toto* without rupturing it.

Pathological report: epidermoid cyst, filled with keratinized dead epithelial cells.

The postoperative course was entirely uneventful. Check up examination, 2 months after operation, revealed no abnormal findings except for an absent right ankle reflex. The patient had no complaints.

**CASE 2** History of three back injuries. Syndrome of cauda equina lesion. Herniated nucleus pulposus (between third and fourth lumbar vertebrae) or traumatic arachnoiditis was suspected clinically. Myelography revealed tumor between third and fourth lumbar vertebrae. Intra arachnoid epidermoid found at operation. Removal with practically complete recovery. R. M., No. 452,881, male, aged 47 years, referred by Dr. W. Mertaugh, Sault Ste. Marie, Michigan, was admitted to hospital November 13, 1939.

Five or 6 years prior to admission, the patient suffered a severe back injury in a toboggan accident. For several weeks he had severe backache and pains in both legs. Even after recovery from the acute symptoms, a dull ache in the lumbar spine and pains in the legs persisted, especially on exertion. Four years prior to admission, patient sustained another back injury (automobile accident). He required 5 weeks' hospitalization and a diagnosis of fractured lumbar spine was made. There was in addition radiation of pain along the course of the left sciatic and of the right crural nerve.

Two years prior to admission, the patient suffered a third back injury, when he fell on a steel plate. His left leg became immediately paralyzed for 15 minutes, and he experienced severe pain in the left groin. On admission, the patient complained of persistent backache in the lumbar region, shooting pains radiating to the anterior surface of both thighs, worse on the left, and also of left sciatic pain. The pains were aggravated by movements or by coughing. During the past 8 years increasing constipation had been noticed.

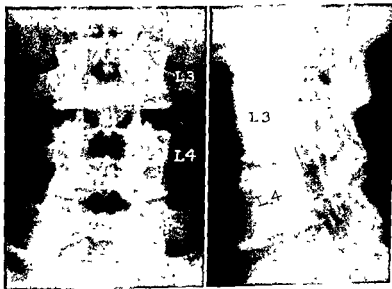


Fig 2. a and b, Air myelogram, Case 1. Epidermoid at third lumbar vertebra.

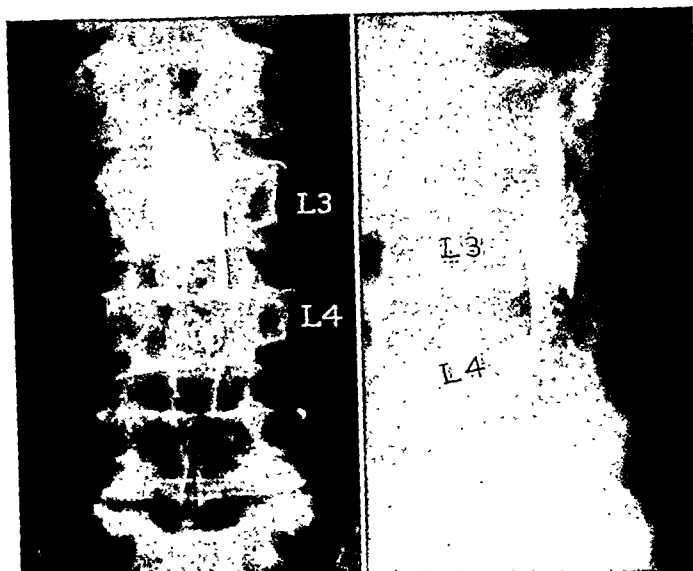


Fig. 3. a and b. Lipiodol-myelogram, Case 2. Epidermoid at third and fourth lumbar vertebrae.

On examination the patient stood with a rigid, anteflexed posture, the normal lumbar lordosis being effaced. There was considerable spasm of the erector trunci bilaterally, with marked limitation of all low back movements. Lasègue's sign was strongly positive bilaterally, and sharp pain was elicited also on stretching the crural nerves. There was paresis of left anterior thigh muscles with considerable diminution of the left knee reflex. All other reflexes were normal. Tactile hypesthesia and hypalgesia were present in the left second lumbar to second sacral dermatomes, and vibratory sensation was diminished in the left foot. The neurological examination was otherwise normal, except for horizontal nystagmus.

Lumbar puncture, done in the lateral position, revealed so low a spinal fluid pressure that it could not be measured nor could the effect of jugular compression be determined. The clear, colorless spinal fluid contained 1 lymphocyte per cubic centimeter; Pandy was strongly positive; goldsol 000110000; total protein, 108 milligrams per cent.

Roentgen-ray examination of the spine showed hypertrophic arthritic changes in the lumbar region, but no evidence of fracture.

Myelography with lipiodol, injected by lumbar route, showed complete obstruction of the spinal canal at the level of the fourth lumbar vertebra. Above the obstruction the mottled flaky surface of an intradural tumor was outlined which extended upward to the level of the intervertebral disc between the third and fourth lumbar vertebrae. (Fig. 3c and d).

Diagnosis: While clinical history and findings favored the diagnosis of posttraumatic arachnoiditis of the cauda equina or of rather high herniation of the nucleus pulposus on the left (between third and fourth lumbar vertebrae), myelography suggested intradural tumor with associated arachnoiditis. A meningioma was suspected.

Operation was performed by Dr. C. F. List, on November 30, 1939, under avertin-ether anesthesia. The posterior

laminae of the third, fourth, and fifth lumbar vertebrae were removed and also the left inferior articular facet of fourth lumbar vertebra, which protruded abnormally into the spinal canal, as if it had been previously fractured and dislocated. The hypertrophied ligamentum flavum between fourth and fifth lumbar and between fifth lumbar and first sacral vertebrae was also excised. When the dura was opened, an intra-arachnoid, ivory white, soft caseous epidermoid, the size of a date was encountered. The tumor extended from the level of the third to fourth lumbar vertebra. Its avascular capsule was exceedingly thin and firmly adherent to roots of the cauda equina on the left.

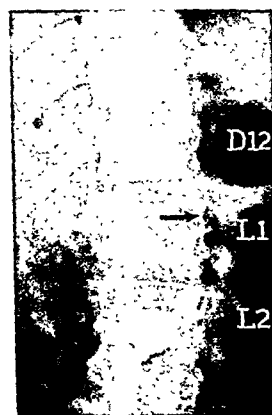


Fig. 4. Lipiodol myelogram, Case 3. Dermoid extending from twelfth dorsal to second lumbar vertebra. Note enlargement of spinal canal at that level. Arrow points to a markedly atrophic pedicle.

There were many dense arachnoid adhesions even beyond the confines of the tumor. Because the friable tumor capsule could not be separated from the nerve roots without damage, a complete intracapsular removal of the epidermoid contents was performed and then as much of the capsule was resected as possible.

Pathological report: epidermoid consisting of desquamated keratinized epithelium.

Postoperative course was uneventful except for temporary retention of urine, requiring indwelling catheter for 2 weeks.

Check up examination, 7 months after operation revealed the following. The patient stated that his pains disappeared immediately after operation and never returned. He walked, moved about, and even danced without discomfort, but still complained of slight constipation. Examination showed almost normal range of back movements, negative Lasègue, no muscular weakness, but slight atrophy of left thigh. There was marked diminution of the knee reflex and slight diminution of adductor and ankle reflex on the left. Mild hypalgesia was present in the second to fourth lumbar dermatomes on the left.

## 2. Dermoid

**CASE 3.** Syndrome of cauda equina lesion with marked signs of local meningeal irritation. Roentgenological evidence of intradural tumor extending from the twelfth dorsal to second lumbar vertebrae. Almost complete removal of partially intramedullary dermoid of cauda equina and conus terminalis. Recovery with residual cauda equina syndrome. Considerable late functional improvement after secondary orthopedic operations. T. A., No. 432,216, female, aged 8 years, referred by Dr. J. T. Jerome, Traverse City, was admitted to the hospital October 13, 1938.

Three years prior to admission, the child complained of occasional pain in her right hip, exaggerated by straining. For more than a year she also experienced dull backaches in the midline of the upper lumbar region. This pain was eased by walking about and aggravated by exertion. Recently it increased in intensity and became almost continuous. In the last months prior to admission, the child assumed a peculiar twisted posture of her back, urination became difficult to start, and there were complaints of constipation and of tingling sensations in both feet.

On examination, the child stood with a rigid lumbar spine and slight list to the right. Severe muscle spasm of the long back muscles prevented flexion and extension movements, especially of the low dorsal and upper lumbar spine, where as lateral inclination was less limited. There was marked local tenderness of the first and second lumbar spinous processes, coughing, jugular compression or even flexion of the neck produced nonradiating pain in the same location. Some stiffness of the neck was present, this was thought to be a protective muscle spasm to prevent transmission of movement to the upper lumbar spine. The right calf muscles were slightly atrophic. Bilateral mild equinus posture and hypotonicity of the feet were noted. Lasègue's sign was strongly positive on both sides. There was slight weakness of long toe extensors, toe flexors, peronei, and of hamstring muscles bilaterally. Patellar and gluteal reflexes were diminished, ankle, hamstring, and plantar reflexes were absent bilaterally. Sensory or sphincteric disturbances were absent. Bilateral horizontal nystagmus was also noted.

Lumbar puncture, done by the referring physician, revealed a clear colorless fluid under pressure of 205 millimeters water. On jugular compression, there was partial manometric block. Cell count was 31, type of cell not specified, Pandey, strongly positive, and goldsol, 0.000017210.

Roentgen ray examination showed definite increase of the anteroposterior and transverse diameter of the spinal canal, at the level of the twelfth dorsal, first and second lumbar vertebrae. Also the pedicles and posterior margins of the bodies of these vertebrae showed erosion from pressure.

Myelography, with lipiodol, injected by lumbar route, revealed complete obstruction of the spinal canal at the superior margin of the second lumbar vertebra with "cupping" of the lipiodol, suggestive of intradural tumor (fig. 4).

Diagnosis was made of a slowly growing tumor, located in the conus region and upper portion of the cauda equina, corresponding to the bony level of twelfth dorsal to second lumbar vertebra. The tumor was thought to be a neurinoma or an ependymoma of the filum terminale.

Operation was performed by Dr. S. Braden, on October 23, 1938, under avertin-ether anesthesia. The posterior laminae of the twelfth dorsal, first, second, and third lumbar vertebrae were removed. The first and second lumbar laminae were found to be markedly thinned, the epidural fat absent at this level and the dural sac enlarged. After the dura was opened, a smooth whitish dermoid of sausage shape and the size of a thumb was seen within the arachnoid, displacing the roots of the cauda equina anteriorly. The lower pole of the tumor was free, yet some nerve roots were firmly adherent to its avascular capsule. The dermoid consisted of two main masses which were connected by a narrow bridge of fibrous and adipose tissue. The upper pole of the tumor had an intramedullary location within the conus and epicurus from which structures it could not be dissected without causing damage. Therefore, the capsule of the dermoid was incised and complete enucleation of the sebaceous material containing some hair was performed. The collapsed remnants of the capsule were folded in and sutured to prevent contamination of the subarachnoid space with free sebaceous material.

Histological report: Cyst wall consisting of cornifying stratified squamous epithelium, a few accessory skin structures, dead hairs and desquamated keratin in the lumen—a dermoid cyst.

Postoperative course was stormy with fever and signs of meningeal irritation lasting a week. Complete paralysis of the bladder developed necessitating indwelling catheter, the pareses of the lower extremities were increased also. Cystometric examination, one month after operation, revealed a combination of reflex and autonomous bladder.

Check up examination, 18 months after operation, disclosed a rather marked cauda equina syndrome with greater involvement on the right. There was calcaneus deformity of the right foot, atrophy and weakness of the right toe extensors, gastrocnemius, hamstring muscles, and gluteus maximus. The left knee reflex and both ankle and hamstring reflexes were absent. There was surface hypesthesia and hypalgesia in the fifth lumbar to fifth sacral dermatome on the right. The disturbance of vesical function, characterized as "autonomous neurogenic type" was still present, but the patient kept herself fairly dry. A triple arthrodesis of the right foot with transplantation of peroneal muscles improved the patient's gait.

## 3. Dermal Sinuses

**CASE 4.** Thirteen years' history of intermittent weakness of the legs and of an occasionally discharging pilonidal sinus in the upper dorsal region. One brother had a pilonidal sinus of the sacral region. Findings suggested intramedullary spinal cord tumor in the upper dorsal region. Operation revealed dermal sinus above the third dorsal spinous process extending through the dura into the spinal

cord. Complete removal of hair-containing, sebaceous, intramedullary mass, extending from the first to fifth dorsal segment. Marked improvement with mild residual cord symptoms, unchanged after 4 years' observation. D. D. C., No. 381,180, male, aged 19 years, referred by Dr. H. B. Haynes, Lansing, Michigan, was admitted to the hospital May 4, 1936.

At the age of 6, 13 years prior to admission, the patient noted a slight weakness of the right leg. Half a year later, the left leg also became affected and, within a few months, the left leg became weaker than the right one. Twelve years prior to admission, the patient was examined in another hospital. A mild spastic paraparesis of the legs without sensory changes was then found. Roentgenograms of the spine were said to be normal. Spinal fluid examination showed 15 white blood cells (unspecified), increased globulin and mastic reaction was 33100000. Four years prior to admission, the function of the legs improved so remarkably after chiropractic treatment that the patient was not only able to walk well, but also to play football. He merely noticed slight stiffness of the legs on exertion. Two years prior to admission, however, the weakness of the left leg recurred and the right leg became involved in the last few weeks prior to admission. The patient also stated that he could not always tell "where his left foot was," that he had become constipated and had difficulty initiating urination.

Since earliest childhood the patient was known to have a hair-containing dimple in the upper portion of his back. Occasionally, this area discharged and became red and sore to touch, with radiation of pain to the shoulder blades. The soreness disappeared whenever some of the hair tuft was removed. The patient stated that one brother had a pilonidal cyst removed from the sacral region.

Examination revealed a dimple in the midline between the second and third dorsal spinous process, containing a small tuft of hair. Palpation revealed a deep induration which was tender to pressure, extending from the dimple upward and paravertebrally toward the base of the second spinous process which was also tender.

Neurological examination revealed definite paresis of the left intercostal muscles below the third interspace and of the left abdominal muscles which occasionally exhibited peculiar spontaneous clonic contractions. The right upper abdominal reflex was diminished; all others were absent. The left foot assumed a varo-equinus posture. There was moderate spastic paraparesis of the legs. The paresis was of the so called predilection type and more pronounced on the left. The deep reflexes of the lower extremities were exaggerated with clonus, Babinski and Oppenheim bilaterally. Pain and temperature sensations were diminished in the third and fourth dorsal dermatomes bilaterally, and below this level considerable reduction of all modes of sensation was present, especially on the left. Vibratory sensation of the legs and position sense of the toes were diminished on the right and absent on the left. The patient walked with a spastic-atactic gait, the disturbance being greater on the left. There was fall tendency in the Romberg position.

Lumbar puncture, done in the recumbent posture, showed clear xanthochromic spinal fluid with an initial pressure of 165 millimeters water. On jugular compression, there was almost complete manometric block. After removal of 4 cubic centimeters of fluid the pressure dropped to 0. No cell count could be done because of artificial slight admixture of blood. Pandy and Nonne were strongly positive. Goldsol, 022123332100. Mastic, 123321. Kahn, negative.

Roentgen-ray examination revealed definite widening of the spinal canal at the level of the first to third dorsal vertebrae, with thinning of the left pedicles. There was a spina bifida of the first sacral segment.

Myelography, with lipiodol, introduced by lumbar route, showed complete obstruction of the spinal canal at the lower margin of the third dorsal vertebra.

Diagnosis was made of a probable intramedullary cord tumor occupying the upper dorsal segments. The tumor was thought to be a dermoid connected with the pilonidal sinus.

Operation was performed by Dr. M. M. Peet, on May 11, 1936, under avertin anesthesia. The stalk of the pilonidal sinus was found to be surrounded by scar tissue, apparently resulting from previous infection. The sinus tract extended through the intervertebral space between the second and third dorsal vertebrae. After removal of the laminae of the seventh cervical to the fourth dorsal vertebrae the dermal sinus was seen to penetrate dura and leptomeninges and to terminate within the cord (Fig. 5). The widened spinal cord formed a mere shell around a large intramedullary mass consisting of sebaceous material and a few hairs. As far as could be determined, the intramedullary tumor, which measured 10 centimeters in length, was completely removed.

On histological examination, a cross-section of the deeper, extraspinal, portion of the excised dermal sinus (Figs. 6 and 7) showed a central lumen lined with stratified squamous epithelium, hair follicles, and sebaceous glands. The mesenchymal layer of the dermal sinus was surrounded by a covering of meninges, consisting of arachnoid with psammoma bodies and dura. Various parts of the dermal sinus showed infiltration with pyogenic granulation tissue. The intramedullary mass consisted of dead keratinized epithelium and sebaceous material.

Postoperative course was rather stormy for 9 days with temperature elevation to 104 degrees F., but without severe meningeal signs.

Check-up examination. A sweating test (heat method) done 3 months after operation showed marked hypohidrosis below the fourth dorsal segments bilaterally, but relative hyperhidrosis above this level (Fig. 8).

Re-examination, 4 years and 4 months after operation, revealed a residual Brown-Séquard syndrome with mild spastic paresis of the left leg and trunk, disturbance of deep sensation in the left leg and diminution of pain and temperature sensation on the right below the fifth dorsal segment.

CASE 5. Symptoms and signs of acute *Bacillus coli* meningitis and, later, epidural abscess in the lumbar region. Lumbosacral pilonidal sinus. Operation showed cylindrical body of epidermoid material embedded in the dura, surrounded by epidural and subdural abscess. Open drainage. Recovery with residual cauda equina syndrome. Late improvement after orthopedic operations. D. W., No. 368,169, female, aged 7 years, referred by Dr. G. J. Prout, Saline, Michigan, admitted September 3, 1935.

The child developed severe headaches 3 days prior to admission. The following day there were nausea and vomiting, and retraction of the head also developed.

Examination, on the Contagious Unit of the Pediatric Department, revealed the following: The child was acutely ill with flushed skin. Temperature was 101.4 degrees F.; pulse, 96; respirations, 24. There was stiffness of the neck and back with positive Brudzinski and Kernig signs. Knee and ankle reflexes were diminished.

Lumbar puncture showed the spinal fluid under increased pressure, cell count was 1400, 95 per cent of which were neutrophil leucocytes, 5 per cent lymphocytes. Pandy and Nonne were strongly positive; goldsol, 0022210; mastic, 242110. The smear showed no organisms and the culture no growth.

Diagnosis of acute meningitis was made, the etiology of which was undetermined.

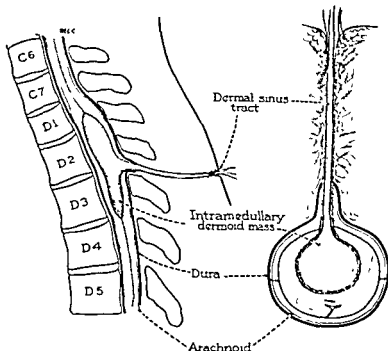


Fig 5. Case 4. Semidiagrammatic drawing to show the topographic relations of the dermal sinus. At left, midsagittal section, at right, cross section, showing the meningeocele, surrounding the deep portion of the dermal sinus.

Further course in the hospital. The patient's condition grew worse on the second day. The fever rose to 104 degrees F, the pulse to 128, and respirations to 38. The meningeal signs increased. Cisternal puncture then showed 430 polymorphonuclear leucocytes. Culture and smear revealed *Bacillus coli* and, in the smear only, gram positive diplococci. Two days later, urinary retention occurred. Again *Bacillus coli* and diplococci were grown from the spinal fluid obtained by lumbar tap. In the following 2 weeks, an irregular fever of 101-102 degrees F and signs of meningitis persisted. Repeated cell counts of the spinal fluid showed a slight drop of cells (average 250) with a greater percentage of lymphocytes. Colon bacilli were repeatedly demonstrated, not only in the spinal fluid but also in the catheterized urine.

On the twentieth day of hospitalization, the temperature again rose to 101.4 degrees F. When lumbar puncture was attempted between the second and third lumbar vertebrae 3 cubic centimeters of foul smelling pus was evacuated before the dura was penetrated, culture of which again showed *Bacillus coli*. Cisternal puncture on the same day yielded clear fluid, containing only 65 white cells, 50 per cent of them being neutrophils and 50 per cent lymphocytes.

Diagnosis of epidural abscess in the lumbar region was made and the patient was transferred to the neurosurgical service. On questioning, the child had complained of numbness of the legs and abdominal distention for the past 2 days.

Repeated neurologic examination showed in addition to the marked meningeal signs, paresis of the distal seg-

ments of both lower extremities with loss of ankle reflexes but no sensory changes could be demonstrated. Another

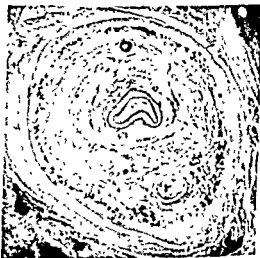


Fig 6. Case 4. Photomicrograph of cross section deep portion of dermal sinus. General view at low power.

finding was considered of significance: In the midlumbosacral region, a small reddened dimple was present, with a tuft of hair, apparently an infected pilonidal sinus.

It was then suspected that the dermal sinus tract extended into the vertebral canal, thus serving as portal of entrance for the infection of the epidural and subarachnoid space.

Operation was performed by Dr. S. Braden on the same day—September 3, 1935—under nitrous oxide anesthesia. As the lumbar muscles were stripped from the spine, foul-smelling pus was encountered at the level of the third lumbar vertebra. Laminectomy of the second to fourth lumbar vertebrae disclosed a large epidural abscess. Two small cylindrical bodies were then seen embedded in the dura; they had a shiny surface with a pearly luster and consisted of soft cheesy material (Fig. 9). The operative note mentions no connection of these structures with the cutaneous dimple. After removal of the epidermoid bodies, pus escaped also from within the dura. After the dural opening was enlarged, a subdural abscess was exposed, the cavity of which measured 5 centimeters in length. The thickened and inflamed arachnoid was left intact. The wound was left open and packed with gauze soaked with metaphen in oil.

On microscopic examination, the cylindrical pearly structures consisted of dead lamellated cornified epithelium showing at one area a narrow lining of viable epithelial cells and polymorphonuclear leucocytes—an infected dermal sinus.

Immediately after operation the temperature returned to normal. Within 2 months the operative wound healed by granulation. The child developed a "cord bladder" with incontinence, saddle anesthesia, and a left talipes

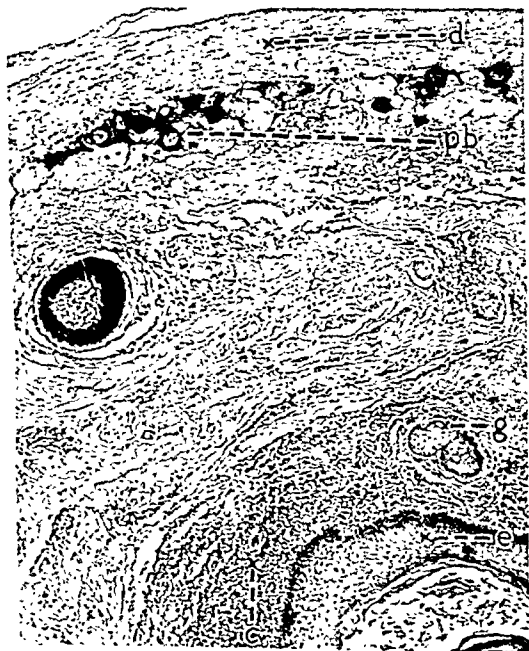


Fig. 7. Higher magnification. *e*, Epidermal layer; *c*, dermal layer, with cellular infiltration; *g*, sebaceous gland; *a*, arachnoid; *pb*, psammoma bodies; *d*, dura.

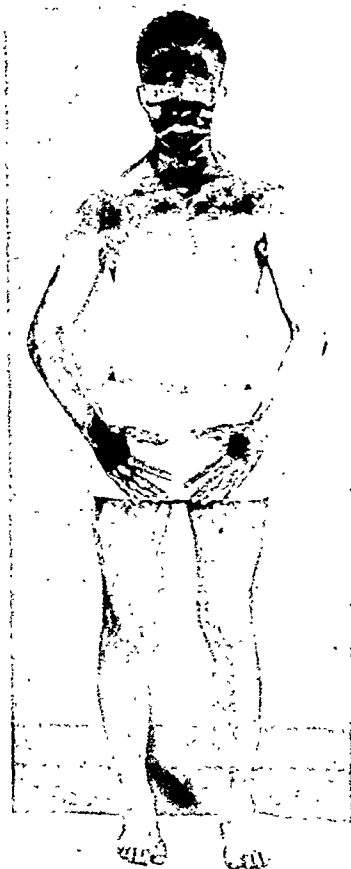


Fig. 8. Case 4. Sweating test (iodine-starch method) shows hypohidrosis below the third dorsal segment.

equinovarus, which was corrected by subsequent orthopedic operations.

Check-up examination, 4 years and 7 months after laminectomy, showed the child to be in good general health. Function of the left foot was much improved. There was still a "neurogenic bladder" with urinary infection, but the patient could keep herself fairly dry.

#### ANATOMICAL AND EMBRYOLOGICAL CONSIDERATIONS

Survey of the literature and of the aforementioned 5 cases reveals a total number of 56 cases, viz. 23 cases of single epidermoid, 19 cases of single dermoid, 3 cases of multiple epidermoids and dermoids, and 11 cases of dermal sinus<sup>1</sup> with intraspinal extension.

This group, taken as a whole, shows preferential location in the lower portion of the spinal

<sup>1</sup>The most common variety of dermal sinus (pilonidal sinus or cyst), which is situated in the sacrococcygeal region and usually has no meningeal connection, is considered beyond the scope of this paper.



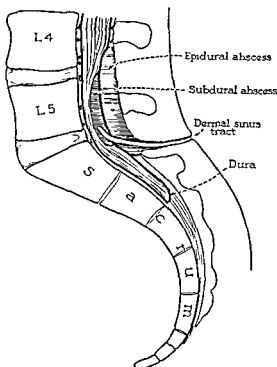


Fig. 9 Semidiagrammatic drawing of dermal sinus, Case 5, to show epidural and subdural abscess. The epidural abscess was more extensive than pictured here.

canal: 35 cases, below the twelfth dorsal vertebra, 62 per cent. Only in one single instance (Mixer), the lesion originated in the cervical spine, in another exceptional case (Ivanoff), it extended throughout the entire length of the cord up to the medulla oblongata.

More pertinent information is obtained by considering the three types of dermal formations individually, and by dividing them into lesions of (1) the cervical cord, (2) the upper thoracic portion of the cord, (3) the lower thoracic cord, (4) the lumbosacral cord—epiconus and conus—and (5) the cauda equina and filum terminale (Fig. 10). Epidermoids are then found to exhibit fairly uniform distribution over the upper dorsal, 4 cases; low dorsal, 6 cases, and lumbosacral portion of the cord, 5 cases, but their incidence is somewhat higher at the level of the cauda equina, 8 cases. Dermoids show a striking preference for the lumbosacral portion of the cord, 12 cases, (see Fig. 1b), but are less commonly confined to the cauda equina, 4 cases. They are rare in other locations: cervical, 1 case, upper thoracic, 2, low thoracic, 1. Dermal sinuses are found either in the

upper thoracic area, 4 cases, or in the distal parts of the cauda equina, lumbosacral portion of the spine, 6 cases, whereas they appear to be rare at other levels, 1 case in low thoracic region.

An attempt was made to group these lesions according to their relationship to the meninges as extradural, subdural, subarachnoid, subpial and intramedullary. Unfortunately, such classification must remain inaccurate, because descriptions in the literature sometimes lack detail, or because it may be impossible to determine the exact origin of a large tumor. Giving due consideration to these reservations, it may be stated that almost two-thirds of all lesions were situated within the leptomeninges, one-fifth frankly intramedullary and the few remaining ones confined to the extradural space. Epidermoids, especially those occurring in the thoracic region, were often found to be intramedullary. Dermal sinuses infrequently penetrate as far as into the cord itself, but usually end in the epidural or subdural spaces. It may be mentioned here, that the superficial parts of a dermal sinus assume the histological characteristics of external skin, whereas the deep cul-de-sac may possess no cutaneous appendages and hence resemble an epidermoid.

Most lesions exhibited preference for the posterior circumference of the cord, a fact of pathogenetic significance: cases of Fraser, Schroeder, Harriehausen, Michelsen, Mixer, and others.

There exist three observations of multiple epidermoids and dermoids within the spinal canal: Trachtenberg, Raymond, Alquier, and Courtellemont, and Muscatello. Bostroem and others described an occasional tendency of both dermoids and epidermoids to form "daughter" nodules, presumably due to rupture of the thin capsule of the main mass. Such rupture of the growth probably caused widespread dissemination of cholesteatomatous material over the entire subarachnoid space in Trachtenberg's case—primary dermoid of the lumbosacral cord—and Raymond, Alquier, and Courtellemont's case—probably primary dermoid of the frontal lobe. On the other hand, epidermoids and dermoids may be primarily multiple as in Muscatello's case which will be discussed later.

Embryological investigation furnishes the clue to the pathogenesis of epidermoids, dermoids, and dermal sinuses. A generally accepted theory (Bostroem, Critchley and Ferguson, Walker and Bucy) assumes that these formations arise from displaced cutaneous-ectodermal cell inclusions. This heterotopia is thought to occur in early fetal life, probably in the third to fifth week. During this period, the neural groove closes to form the

medullary tube and the ectoblast differentiates into cutaneous and neural ectoderm. Cutaneous ectodermal cells may then be trapped either within the neural tube or near the closing medullary folds and thus become the first *anlage* of intramedullary or paramedullary epidermids or dermids. If the cleavage of cutaneous and neural ectoderm remains incomplete at a certain point, a dermal sinus will develop connecting the external skin with the neuraxis. This theory is well supported by von Verebely's case. There was a large extradural tumor in the lumbar portion of the spinal canal, consisting of 2 separate cysts. The inner cyst was neuroepithelial in type, betraying its origin from the neural ectoderm; the external cyst, however, was a dermoid derived from the cutaneous ectoderm.

Whether a dermoid or epidermoid will develop depends, in the opinion of most authors, upon the period during which the cell inclusion occurred. If it happened very early in fetal life, the displaced cells are still completely potential and able to form a dermoid; if, at a later period, the cells have already undergone partial differentiation and become unipotential, an epidermoid will develop. Other authors believe that a dermoid results from displacement of cells belonging to all cutaneous layers, whereas an epidermoid is derived from epidermal cells only. Strictly speaking, dermids may be considered as bigerminal teratoid formations. There exist also transitional forms between dermids and true teratomas.

Knowing their mode of origin, we now understand why epidermids, dermids, and dermal sinuses so frequently occur in the midline or at the posterior circumference of the cord. Evidently, these lesions are associated with a disturbance in the "posterior closure line" of the neuraxis and sometimes of the vertebral canal as well. A few examples, selected from the literature, will show that the dermal formations under discussion may be classified with the so-called dysraphic disorders. In Harriehausen's and Hamby's cases a posteriorly situated dermoid of the lumbosacral cord marked the beginning of a complete diastematomyelia. In Fraser's and in Salotti's cases, tumors in the posterior median sulcus produced a deep groove which, according to these authors, suggested rudimentary duplication of the cord. Most instructive of all is Muscatello's case. His patient showed a wide posterior rachischisis of the third to tenth thoracic and fourth and fifth lumbar vertebrae. An extradural dermoid was present at the level of the fourth thoracic vertebra, and a small epidermoid at the level of the fourth and fifth lumbar vertebrae. Furthermore, there was

hydromyelia and diastematomyelia. This case, then, demonstrates a combination of multiple dysraphic disorders of the cord and spine with two congenital tumors. It is also worthy of mention that spina bifida occulta is frequently present at the level of a dermal sinus: cases of Walker and Bucy, Ottonello, Ripley and Thompson, Moise, Sharpe, and Hipsley. The dysraphic character of the dermal sinus is clearly shown in our Case 4, even though no spina bifida existed. Here, the deeper portion of the sinus tract was surrounded by a meningeal covering (meningocele) containing dura and leptomeninges with psammoma bodies (Figs. 6 and 7).

Recent embryological work dealing with the development of the lower part of the spinal cord (Holmdahl) and of the filum terminale (Streeter) may give some explanation as to why dermids and also epidermids occur preferentially in the distal portion of the neuraxis. Holmdahl casts aside the orthodox view that the neural tube is exclusively formed by ectoderm. He points out that the caudal part of the neural tube develops directly from an undifferentiated cell mass not belonging to any particular germinal layer. According to this author, the low thoracic and entire lumbosacral portion of the human cord are formed in this manner, which he terms "secondary phase of body development" in contrast to the primary phase of development from germinal layers. Holmdahl's findings would readily explain the relative frequency of dermids and other dysembryonic tumors (teratomas) in the lumbosacral portion of the cord, since one has only to assume that disorderly differentiation of the primitive matrix causes these tumors.

Streeter's work on the development of the filum terminale is based on the fact that the vertebral column grows much more rapidly than the spinal cord. As a result, the distal end of the cord finally corresponds to the upper border of the second lumbar vertebra. The coccygeal segments of the cord become elongated to the filum terminale and the nerve roots to the cauda equina. A process of dedifferentiation transforms the coccygeal segments into the filum terminale. Since the distal—coccygeal—end of the cord is originally attached to the cutaneous ectoderm, it is evident that dermal inclusions may easily occur at that point. In later phases of embryonic development, the heterotopic dermal material keeps its close topographic relation to the distal end of the cord—filum terminale—and hence becomes situated in the upper lumbar portion of the vertebral canal, a preferential location for both dermids and epidermids. The presence of dermal inclusions dis-

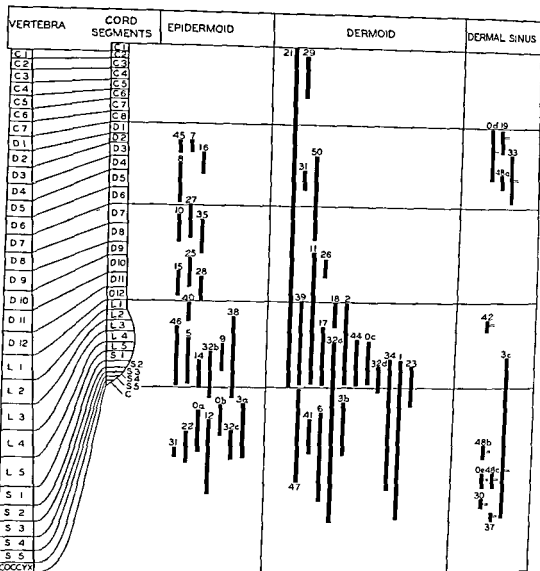


Fig 10 Diagram to show the location and size of epidermoids, dermoids, and dermal sinuses, in relation to the spinal cord segments and to the vertebrae. Numbers indicate the authors which appear in the appended bibliography.

turbs the normal dedifferentiation of the coccygeal segments to the filum terminale, thus, in 2 cases of dermoid (Bradford, Pitotti) (Fig 1b), the sacral portion of the cord, involved by tumor, actually extended down to the sacrum as it does in early fetal life. In Boldrey and Elvidge's second case, there was anomalous dilatation of the ventriculus terminalis above the dermoid.

phy, letters after the numbers are used when the author described several cases. O, a to e designates our own cases. Cross bars in the group of dermal sinuses indicate the level of the sinus tract.

#### CLINICAL AND DIAGNOSTIC CONSIDERATIONS

*Incidence as to sex and age, duration of symptoms.* Epidermoids appear to be more frequent in the male—15 male, 8 female, whereas dermoids and dermal sinuses are about equally distributed in both sexes—16 male, 14 female.

It is customary to chart a disease according to its incidence in various age groups. That method

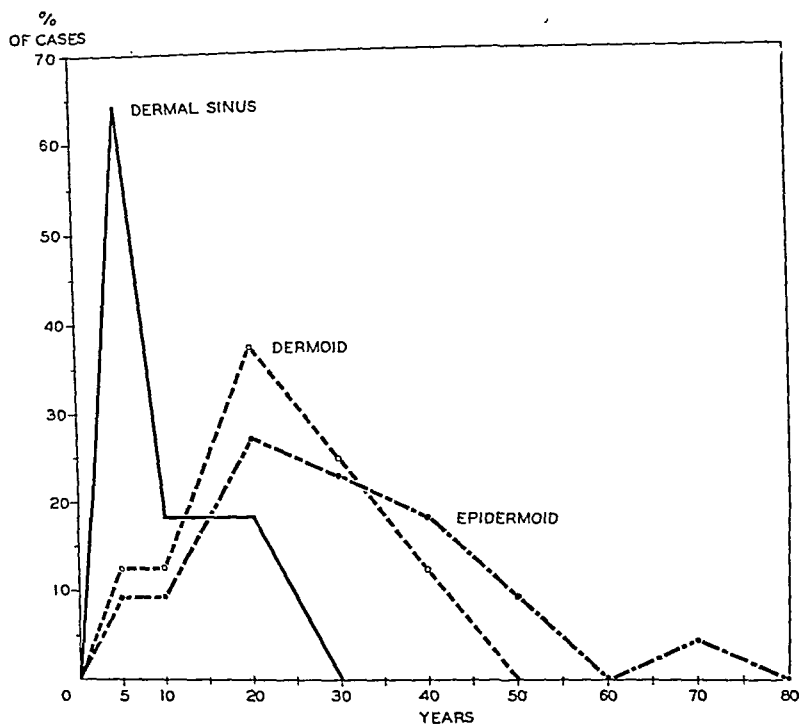


Fig. 11. Graph to show the frequency with which epidermoids, dermoids, and dermal sinuses become clinically manifest in various age groups.

is apt to be misleading in epidermoids and dermoids, because these extremely slow growing tumors are present, though latent, from birth. They may come under observation at any stage, even before causing clinical symptoms; they were accidental autopsy findings in the cases of Muscatello and Lauterburg. Their natural course may last over the entire span of life. It is, therefore, preferable to group them according to the age at which the first clinical symptom appeared. As shown in the graph (Fig. 11), the majority of dermal sinuses become clinically manifest within the first decade, in fact usually before the age of 5, because of their tendency to become infected. Dermoids cause their first symptoms within the first two decades, especially in the late adolescent period. Epidermoids are slightly slower to develop; as a rule they become manifest in the early adult period, but may cause their first symptoms any time between the ages of 20 and 50. After the age of 50, both epidermoids and dermoids rarely occur, yet in a patient of Bouchut, Dechaume and Michailidis, the first symptom was noted at 61; death at 71. The average age of 22 patients with epidermoids was 29.8 years, their first symptom

occurred at 23.5 years, hence the observed duration of symptoms was 6.3 years. In 16 dermoids the average age was 28.3 years, the first symptom occurred at 18.7 years, and the duration was 9.6 years. These figures emphasize the extremely slow rate of growth in both groups. A course over 10 years is not unusual, and in 2 instances—Case 1 of Naffziger and Jones, and in the case of Verbiest the patients were known to have shown symptoms for 42 and 43 years, respectively. That dermoids become manifest sooner than epidermoids might be due to the fact that dermoids expand by secretion of sebaceous glands in addition to the mere accumulation of dead epithelial cells which is typical for epidermoids.

A peculiar feature of spinal epidermoids and dermoids is their tendency to long remissions. There were 12 cases with long asymptomatic periods. In Verbiest's case, for example, remission lasted 22 years; in other instances, 10 and 8 years. It is difficult to explain the free interval, as sudden gross variations in size of the tumor are unlikely. Marked improvement during the period of remission may mislead the clinician and cast doubt on the diagnosis of cord tumor.

**Neurological symptoms.** As to neurological symptoms and signs, epidermoids and dermoids differ little from other slowly growing tumors within the spinal canal. The clinical symptomatology largely depends upon the level and extent of the lesion. As in other slowly growing neoplasms, the degree of objective motor and sensory impairment may be amazingly slight in comparison to the magnitude of anatomical damage.

Lesions implicating roots of the cauda equina are often characterized by exceedingly severe signs of radicular and local meningeal irritation which may entirely dominate the clinical picture (Naffziger and Jones, Bagley and Arnold, and my own observation). These patients exhibit marked spasm of the long back muscles with bizarre antalgic postures. Kernig's, Lasègue's, and Brudzinski's signs are strikingly positive. Typical root pain can be elicited by slight jugular compression or movements of the head, especially flexion (Naffziger and Jones, and my own observation). The unusual severity of root pain observed in epidermoids and dermoids has been attributed to chemical arachnoiditis. Considerable local irritation and inflammatory changes are presumably caused by cholesterol crystals (Mahoney) or free fatty acids (Verbiest) contained in these tumors.

In lesions of the thoracic cord, radiculomeningeal symptoms are less prominent; a transverse syndrome suggestive of intramedullary process is often present, since a high percentage of thoracic epidermoids actually are intramedullary. Occasionally, striking disturbances of vegetative functions such as disorders of sweating (our case 4, Fig. 8) may be associated with intramedullary lesions of the thoracic cord.

Dermal sinuses deserve special comment because of their highly characteristic symptomatology. A telltale dimple in the posterior midline, containing a tuft of hair and occasionally discharging sebaceous material, establishes the diagnosis, especially, when neurological symptoms point to the same level. The skin lesion, however, may be so inconspicuous that it is overlooked until the dermal sinus has become infected. Then, there is pain and local inflammatory infiltration and the dimple discharges purulent material. When infection reaches the deeper portion of the sinus, symptoms and signs of epidural or subdural abscess and of meningitis may develop (Walker and Bucy and others). In etiologically obscure cases of meningitis or spinal epidural abscess, therefore, one should always consider the diagnostic possibility of infected dermal sinus as portal of entry for the infection (Moise, Ripley and

Thompson, and others). Dermal sinuses of the lumbosacral area frequently become infected in early childhood, since that region is apt to be contaminated with *Bacillus coli*, pyogenic cocci, and other organisms. Sometimes the patients pass through recurrent episodes of meningitis (Walker and Bucy). Dermal sinuses of the upper dorsal area are less often infected, but since their narrow external opening may easily be obliterated, sebaceous matter continues to accumulate in the deep intraspinal portion of the sinus with resultant compression of the cord.

**Spinal fluid findings.** The changes of spinal fluid found in epidermoids and dermoids do not differ essentially from those of other cord tumors. Pleocytosis is absent even in cases with marked meningoradicular signs. Although the amount of total protein may be considerably increased, it rarely reaches the excessive levels commonly found with neurinomas. In 3 cases in the literature, cholesteatomatous material was obtained by lumbar puncture, thereby verifying the lesion. In Raymond, Alquier, and Courtellemont's case, presumable rupture of a dermoid accounted for generalized dissemination within the subarachnoid space. In a second case, reported by Forestier, Haguenau, and Petit-Dutaillis, an epidermoid at the level of the first and second lumbar vertebrae was accidentally punctured on attempted spinal tap. The same thing happened in a case of lumbar dermoid reported by Boldrey and Elvidge.

Cases of infected dermal sinus show various types of meningitic changes in the spinal fluid. The fluid may be actually infected or sterile, and pleocytosis may be polymorphonuclear or lymphocytic, according to the stage of infection.

**Röntgenographic findings.** Roentgenograms of the spine may reveal widening of the spinal canal at the level of the lesion with atrophy of the pedicles and laminae from pressure. This change possibly is more frequent in the expansive dermoids than in the softer and more easily molded epidermoids. On the other hand, the degree of bony change may depend mainly upon the duration of the lesion.

**Mycelography** is not only helpful in determining the level and size of the tumor, but may sometimes demonstrate finer anatomical details. Thus in Case 1 (Figs. 2a and b), the perfectly smooth ovoid appearance of the tumor suggested the diagnosis of dermoid or epidermoid, because the only moderate increase of total protein seemed to rule out the presence of a neurinoma. In Case 2 (Figs. 3a and b), the mottled and flaky surface of the tumor was visualized by lipiodol. The picture resembled the encephalographic appearance of

cerebral epidermids, described by Dyke and Davidoff. The contrast medium within the subarachnoid space had apparently filled all the small crevasses and clefts of the lamellated surface of the growth.

#### TREATMENT

As epidermids and dermids are benign encapsulated tumors, permanent cure should be expected following their surgical removal, yet results obtained in cases published thus far have been encouraging only in the past 15 years. In most patients mentioned in the older literature, no surgery was done or it was attempted too late. Results have improved remarkably, when patients were operated upon at an early stage and modern neurosurgical methods used, but even now certain factors may prevent complete success. The desirable total removal of the tumor, which alone insures permanent cure, is not always practicable because the thin capsule, which contains viable cells, may be too friable and firmly adherent to the cord and nerve roots. It may be wiser, therefore, in some cases to leave fragments of the capsule behind in order to avoid injury to nervous structures, even though this may mean future recurrence. Another technical difficulty lies in the total removal of intramedullary epidermids and dermids. When dealing with such a condition, surgeons are inclined to be conservative for fear of damaging the cord and hence the extirpation may have to remain incomplete. Nevertheless, even an intracapsular enucleation plus partial removal of the capsule may accomplish long lasting symptomatic improvement. Care should be taken not to contaminate the subarachnoid space with sebaceous material as this may cause considerable meningeal irritation.

When dealing with dermal sinuses, the surgeon is confronted with different problems. The sinus tract should be totally excised. Infected dermal sinuses with complicating epidural or subdural abscess or meningitis require open surgical drainage in addition to removal of the sinus. This procedure is usually followed by rapid disappearance of serious symptoms, even though there may be temporary drainage of spinal fluid through the infected field. Fortunately, the accompanying meningitis is often local and sterile in character and subsides soon after drainage. The surgical treatment of infected dermal sinus is effectively assisted by use of sulfanilamide, sulfathiazole, and similar drugs.

#### SUMMARY

After a discussion of the terminology, 5 cases of intraspinal dermal formations were reported, viz.,

2 epidermids, 1 dermid, and 2 dermal sinuses, bringing the total of similar observations to 56.<sup>1</sup>

Epidermids show a fairly uniform distribution over the thoracic and lumbosacral portion of the cord, but are more frequent in the cauda equina. Dermids have a definite preference for the lumbosacral portion of the cord. Dermal sinuses chiefly occur in the upper thoracic region or in the lowermost portion of the cauda equina. It is exceedingly rare for any of these lesions to be situated in the cervical region.

Approximately one-fifth of all dermal formations are intramedullary, two-thirds are located within the leptomeninges and the few remaining cases are extradural. Epidermids of the thoracic cord are frequently intramedullary.

There are rare cases of multiple epidermids and dermids, either due to primarily multiple origin or due to implantation metastases in the subarachnoid space from rupture of the main nodule.

The pathogenesis of intraspinal epidermids, dermids, and dermal sinuses was discussed with reference to various embryological theories. The relationship of these lesions to the "dysraphic state" was emphasized.

Intraspinal epidermids appear to have a higher incidence in the male, whereas dermids and dermal sinuses show approximately equal distribution among the sexes.

On the average, dermal sinuses become manifest in childhood, dermids in adolescence—before the age of 20—and epidermids cause their first symptoms in early adult life, after the age of 20.

The clinical course of all these lesions is long, sometimes lasting over several decades, and may be interrupted by long remissions.

The neurological symptomatology depends mainly upon location and size of the lesion. If nerve roots of the cauda equina—are implicated, signs of local meningeal and radicular irritation may be very severe, presumably due to accom-

<sup>1</sup>After completion of this paper, the following 4 additional cases reported in the literature came to my attention and I also had an opportunity to observe another case myself, thus bringing the entire number of observations to 60.

King reported a rather typical case of epidermoid of the cauda equina. Stammers described 2 cases of infected dermal sinus, 1 in the lumbosacral the other in the sacrococcygeal area; both showed evidence of meningitis. Hamby published an unusual case of dermal sinus at the level of the third lumbar vertebra, associated with duplication of the lower end of the spinal cord. My personal observation concerned a woman, aged 43 years, who was known to have weakness and deformity of the feet for at least 30 years. After her symptoms had been stationary for 25 years she finally developed a full blown conus syndrome. Lumbar puncture revealed a manometric block on jugular compression and xanthochromic fluid with moderate increase in total protein. The spinal canal was widened at the level of the first and second lumbar vertebrae. At operation, an intramedullary dermoid of the lumbosacral cord was found which had formed multiple intramedullary "daughter" nodules. All these additional cases confirm the statements made in the body of this paper and bring out no further points of special interest. References of the above authors are appended to the bibliography.

panying chemical arachnoiditis. Dermal sinuses are easily recognized by their typical clinical picture. They tend to become infected with resultant epidural and subdural abscess and meningitis.

Changes of the spinal fluid, found in the various dermal formations, are similar to those observed in other intraspinal tumors, although the increase of total protein appears to be less marked than with neurinomas. In rare instances the lesion was directly verified by aspiration of cholesteatomatous material at lumbar puncture. In cases of infected dermal sinus, the spinal fluid may show various types of meningitic change.

Röntgenographic changes of the spine are observed, consisting of widening of the spinal canal. This apparently is more common in dermoids. Spina bifida is frequently found at the level of a dermal sinus. Myelography not only determines the location and size of these lesions, but may give some hint as to the anatomical nature.

The results of surgical treatment of intraspinal epidermoids, dermoids, and dermal sinuses are good, provided they are completely removed. If accompanying arachnoiditis or intramedullary location make such procedure impracticable, intracapsular enucleation may assure long lasting relief. Infected dermal sinuses require excision and open surgical drainage.

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# APPENDICULAR OBSTRUCTION: ITS CLINICAL AND PATHOLOGICAL ASPECTS

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MANY writers, including Van Zwalenburg (6), Wilkie, and more recently Wangenstein and Bowers, have stressed the importance of acute appendicular obstruction as a cause of appendicitis. To be considered a distinct and significant entity appendicular obstruction should possess a characteristic pathological picture and should manifest suggestive clinical symptoms important to the proper diagnosis and prognosis in an individual case. A detailed study of such cases is therefore pertinent to a true evaluation and correlation of clinical evidence and actual pathological findings. This study is based on a group of 70 cases of clinically acute appendicitis in which a factor of obstruction was definitely present. Subjective complaints were determined in most instances by personally questioning the patient several days after operation and the results were compared with the symptoms noted in the pre-operative records so as to make the story thorough and complete. The surgeon's description of the appearance of the operative field was considered the most important estimate of the gross pathological state of the appendix. The majority of these appendectomies were performed by one surgeon who was especially interested in the problem. Gross and microscopic examinations of the appendices were made proximal to, at the site of, and distal to the site of obstruction.

The evidence to be presented in this clinicopathological study will support the contention that acute appendicular obstruction is a distinct pathological entity differing from acute appendicitis that is nonobstructive. Every hollow viscus is subject to at least two types of pathological condition, blockage of its lumen and inflammation of its wall, and the appendix is no exception. Obstruction to the lumen of this organ is comparable to intestinal obstruction in that it may be acute or chronic, partial or complete; yet the structure of the appendix favors the probability of acute complete obstruction in the majority of instances.

The factors which may be responsible for appendicular obstruction are many and varied. The

intraluminal factors which may produce obstruction include fecaliths, fibrous strictures, foreign bodies, lymphoid hyperplasia, and carcinoid tumors. Impacted fecaliths comprise by far the largest percentage of etiological agents, 78 per cent in this group of cases (Fig. 1). Fibrous strictures probably account for the next largest group and often are associated with fecaliths. Fibrotic strictures are manifested by thickening and fibrosis of the submucosa, the same changes which are present as residua following acute or subacute inflammation (Fig. 2). Stricture often is missed owing to proximity to the cecum. Adhesions, secondary to inflammation in the appendix or adjacent organs, kinks, abnormalities of position, and peritoneal bands or membranes, comprise the extraluminal factors of obstruction.

## PATHOLOGICAL PICTURE

Gross examination alone usually provides sufficient evidence to classify a case of acute appendicitis as obstructive or nonobstructive. The circumstances surrounding the organ at the time of operation and its appearance *in situ*, together with a careful examination of the excised appendix, should furnish an etiological factor responsible for the pathological condition. Dilatation of the lumen and thinning of the walls are the two salient features that characterize an acutely obstructed appendix (Fig. 3). The luminal contents are always liquid and under pressure. Passive congestion, acute inflammation, and necrosis are absent in the earlier stages but they successively appear as the pathological process progresses. These changes are even more impressive when the site of obstruction lies distal to the base of the appendix, for then the changes in the appendix distal to the site of obstruction may be contrasted with the normal portion proximal to the site of obstruction, which has a lumen of normal caliber and walls of average thickness. The transition from normal to abnormal may be very abrupt. It is this feature particularly which favors the hypothesis of a primary mechanical etiological agent. Figure 4 shows graphically the anatomical picture at three different levels in the same appendix representing an advanced stage of acute appendicular obstruction.

From the Department of Surgery, the Mayo Foundation.  
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Fig 1 Impaction of fecaliths in the proximal portions of 3 appendices, producing complete obstruction with distal dilatation of the lumina and thinning of the walls.

The increasing pressure of the intraluminal contents distal to the obstruction, the physiological characteristics of which have been described excellently by Van Zwahlenburg (5), Sperling, Burget and co-workers, and Bowers quite naturally produces compression changes in the individual anatomical layers of the appendical wall. These changes are quite typical, and usually the microscopic examination of a single region is enough to establish a diagnosis (Fig. 5). Microscopically we find that the increasing intraluminal pressure has smoothed out the mucosal folds distal to the obstruction, has flattened the columnar cells that line the mucosal surface, has distorted and compressed the mucosal glands into a circumferential axis, has spread apart the individual glands so that there are fewer glands per high power field, has flattened the lymphoid aggregates, and has produced compression and thinning of the submucosa and muscularis.

In studying this series of obstructed appendices it was found that, from the standpoint of pathology, the cases could be classified in two major



Fig 2 a, left, An excised appendix which has been laid open to demonstrate better the abrupt demarcation of normal from abnormal at the site of an obstructing structure. b, A longitudinal microscopic section through the region of stricture showing the intact normal mucosa proximal to the region of fibrous stricture and definite distal thinning of the wall and necrosis  $\times 8$

groups. The first group represents an early stage in which there is a definite obstructive mechanism with typical changes distal to the site of obstruction but no evidence of acute inflammatory infiltration (Fig. 6a). The second group represents the later stage of the process in which acute inflammatory infiltration is present distal to the site of obstruction (Fig. 6b). The only difference between the two groups is complicating infection with acute inflammation and eventual necrosis. One quite logically assumes, therefore, that the



Fig 3 A longitudinal section of an obstructed appendix illustrating a proximal portion in which the lumen is of normal caliber and the walls are of average thickness and free from inflammation, an impacted fecalith with its typical laminated structure, and a distal portion in which there are the characteristic dilatation of the lumen and thinning of the walls. Distally there are passive congestion, acute inflammation, and foci of necrosis. The ease of rupture under these circumstances is evident. Note the abrupt transition from normal to abnormal at the site of obstruction  $\times 1\frac{1}{2}$

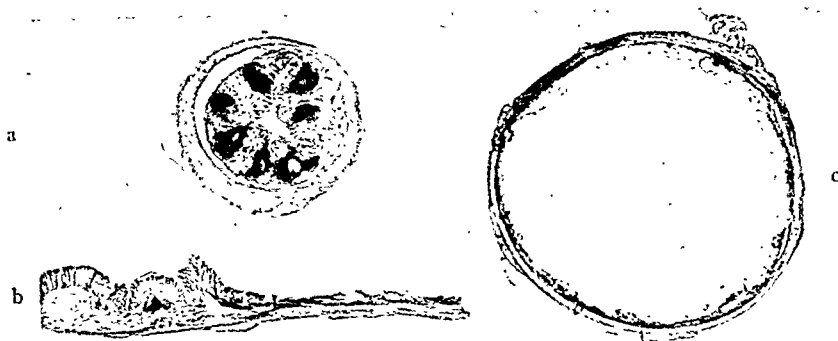


Fig. 4. a, A transverse section through an appendix proximal to the site of obstruction showing perfectly normal architecture free from inflammation and passive congestion.  $\times 3.5$ . b, A longitudinal section at the site of obstruction by a fecalith in the same appendix. Note the abrupt demarcation of normal from abnormal.  $\times 3.5$ . c, A transverse section distal to the obstruction illustrating a markedly dilated lumen and thinned walls which are necrotic, congested and infiltrated with cells characteristic of acute inflammation.  $\times 3.5$ .

second group represents only a later stage in the pathological process. When obstruction becomes complete, the pathological process becomes progressive. The microscopic picture of the organ does not represent a complete description of the disease but only a stage of the disease at the time of appendectomy.

In contradistinction to the preceding picture of an acutely obstructed appendix, the nonobstructive type of acute appendicitis does not show any distention of the lumen or thinning of the walls (Fig. 7). Rather there are thickening and boggi-ness of the walls due to edema and inflammatory infiltration. The muscularis is thick and edematous and its fibers are separated by inflammatory exudate. The mucosal architecture shows none of the aforementioned compressive changes.

#### CLINICAL PICTURE

In studying the clinical history and findings for the entire series it was apparent that the most characteristic symptom in the majority of cases of appendicular obstruction was a colicky type of abdominal pain. The sudden onset of the pain and its intermittence were also suggestive. The intermittent character of a pain is particularly suggestive, for if the initial pain were due to simple infection, the pain would not subside so frequently after a few minutes or hours while the infection continues to extend. Systemic signs of fever, rapid pulse, and leucocytosis may be absent in acute appendicular obstruction even when the pathological picture appears dangerously acute. Yet in the advanced or late stage of the disease they are usually present. This is at variance with the syndrome described by Wilkie and by Boyce

and McFetridge, whose emphasis on the lack of systemic manifestations has led many to suppose that this is characteristic of acute appendicular obstruction. One can say merely that such constitutional signs are usually absent only in the earlier stages and are usually present in the advanced stages. Vomiting is not a characteristic sign of appendicular obstruction; it is as frequently absent as it is present. In all cases some degree of abdominal tenderness was present. The differentiation between acute obstructive and non-obstructive types of appendicitis certainly cannot always be made clinically, but in a very large per-

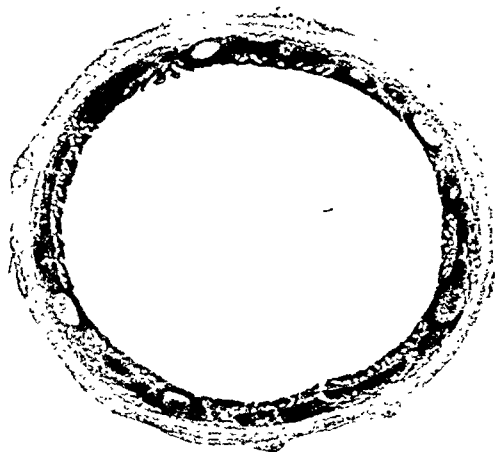


Fig. 5. Transverse section of an appendix distal to the obstruction, illustrating an early phase of acute obstruction with its dilated lumen, thin walls, typical compression changes, and no evidence of acute inflammation.  $\times 7$ .



Fig 6 a, left, The compression changes in anatomic layers of the appendicular wall resulting from increasing intraluminal pressure in the early stage of appendicular obstruction. Smoothing out of the mucosal folds, flattening of the surface epithelium, compression of the mucosal glands into a circumferential axis, spreading apart of the

individual glands, flattening of the lymphoid aggregates and compression of the submucosa and muscularis are all evident  $\times 25$ . b, A transverse distal section in an advanced stage of acute appendicular obstruction showing the necrosis, acute passive congestion, hemorrhage, thrombosis and acute inflammatory exudate  $\times 25$

centage of cases the symptoms are suggestive enough to make one strongly suspect that the obstructive variety is present.

#### REPORT OF CASES

The following reports of cases are illustrative. The first two are typical of the group of early cases of acute appendicular obstruction before bacterial invasion and inflammation complicate the picture. In Case 1 at operation with the appendix *in situ* the impression of the surgeon was that of an acutely obstructed appendix. Microscopic examination by the pathologist did not reveal any acute inflammation and the condition

was labeled as only chronic, thereby minimizing to the clinician the potential danger of the situation. Given a few more hours in which the obstructive factor could produce more passive congestion, distention, and pressure necrosis, the appendicular walls would be permeated with cells characteristic of acute inflammation and gangrene and perforation would be approaching.

**CASE 1** A man, aged 25 years, experienced the abrupt onset of intermittent colicky abdominal pain 48 hours before operation was performed. There were several intervals of complete freedom from pain. During the last few hours before operation, the pain centered in the right lower quadrant of the abdomen and became more steady. The temperature, pulse rate, and number of leucocytes were within normal range. At operation the appendix was found to be definitely obstructed by a fecalith and distal to the site of obstruction to be distended with liquid fecal contents under pressure. To the surgeon the condition represented acute appendicular obstruction. Microscopically the distal walls of the appendix showed the characteristic changes due to compression, but no cells characteristic of acute inflammation were found.

**CASE 2** A girl, aged 18 years, presented an 18 hour history beginning with an abrupt onset of intermittent cramp-like pains in the lower part of the abdomen with particular extension into the right lower quadrant of the abdomen. Nausea became apparent in a few hours but there was no vomiting. The patient's temperature was 98.5 degrees F, pulse, 85, leucocytes numbered 11,500 per cubic millimeter of blood, 79 per cent were neutrophils. Examination disclosed some tenderness in the right lower quadrant of the abdomen. Appendectomy revealed several fecaliths which were definitely obstructing the distal two-thirds of the organ. Microscopic examination showed proximal transverse sections to be normal. Distal sections revealed a dilated lumen, thinned walls with typical compression changes, and moderate passive congestion and hemorrhages. There was no evidence of acute inflammatory infiltration. Because of this absence of inflammation the pathologist classified the condition merely as chronic appendicitis.

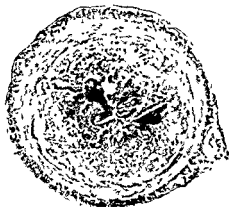


Fig 7 Transverse section through an appendix that is the site of a nonobstructive type of acute appendicitis, illustrating the typical thickening and boggy of the walls which are infiltrated with acute inflammatory exudate. The mucosa has become necrotic  $\times 7$

The next case represents the advanced stage of acute appendicular obstruction wherein bacterial invasion with an acute inflammatory tissue response has been superimposed on the primary picture of acute mechanical obstruction.

CASE 3. A woman, aged 30 years, presented an 18 hour history beginning with an abrupt onset of colicky abdominal pain located always around the umbilicus. The pain was intermittent with several intervals of complete freedom from pain. Temperature, pulse, and number of leucocytes were all elevated above normal limits. Examination revealed slight tenderness in the right lower quadrant of the abdomen and no rigidity. The appendix was found to be acutely inflamed and obstructed in its distal third which was dilated considerably by liquid contents under pressure. Examination disclosed an obstructing stricture in the middle third with a fecalith impacted behind it. Microscopically the transverse sections proximal to the obstruction were normal and intact, whereas distally the walls were compressed and thin, necrotic, and permeated with cells characteristic of acute inflammation and residua of hemorrhage (Fig. 4).

#### OBSERVATIONS

It is apparent, therefore, that appendicular obstruction presents two phases in its development. The first or early phase is that of primary simple obstruction characterized by symptoms suggestive of obstruction and usually with no elevation of temperature, pulse rate, or number of leucocytes. In some instances the obstruction may be partial and occasionally may be relieved spontaneously. The patient may go on with apparently insignificant symptoms for several days before obstruction becomes complete. The rapidity with which the clinical picture develops depends on the completeness and suddenness of the obstruction. The pathological picture corresponds to the clinical manifestations. In the early stage one would not expect and does not find a microscopic picture of an acute process with inflammatory exudate. The late phase begins when the supply of blood to the wall is impaired, owing to increasing intraluminal pressure; then, bacteria begin to invade the wall with resultant acute inflammatory infiltration. Clinically, an elevated temperature and leucocytosis develop. At this stage a diagnosis of acute appendicitis is made easily.

The didactic classification by pathologists of appendices into separate categories, such as "acute suppurative," "simple catarrhal," and "gangrenous," simply portrays the microscopic picture of the organ at the time the surgeon intervened. It must be emphasized again that it is not a description of the disease but of only a stage of the disease at the time of appendectomy. The disease within several hours might have regressed or might have merged rapidly into a more acute

picture, and in the latter instance the microscopic appearance would be very different. This is particularly the case in appendicular obstruction. It is usually a progressive condition, and if the appendix examined by the pathologist shows evidence of only minor changes, it is no criterion that the removal of the appendix was not a vital necessity, for a few more hours might have sufficed to change an innocent appearing structure into a gangrenous one. It is only the early decision of the surgeon based on the clinical picture and his knowledge of possibilities which prevents the change. The speed with which such changes take place is dependent on the completeness of the obstruction and not so much on the duration of the condition.

It should be borne in mind that the microscopic appearance of the appendix is not the sole criterion of the symptomatology. The circumstances surrounding the organ and its appearance *in situ* are often the explanation of the clinical signs and symptoms and the determining factor of what might have happened in a short time. Once these are disturbed one of the most important parts of the story is lost and important facts are concealed from the pathologist, if they are not recorded. The surgeon and the pathologist must co-operate in the study of the etiological factors lest their true significance be lost.

In the obstructive variety of appendicitis the pathological picture is usually progressive. Tension may mount extremely rapidly within the lumen and gangrene and rupture may occur in an exceedingly short time. Time is a much more important factor in the obstructive variety. The average of my advanced series is 24 hours and in most of these cases there were regions of gangrene. Even at the end of 6 hours one specimen showed definite necrosis. Interference with blood supply and increasing intraluminal pressure are the causative factors. If the history is suggestive of acute appendicular obstruction, surgical intervention is urgent. It is reasonable to suppose that rupture of an appendix whose infectious factor has only a short duration is much more serious than that of an appendix which is the seat of a nonobstructive appendicitis in which the infection begins at the onset of the illness and extends over a much longer time. In the latter instance the surrounding peritoneal cavity and omentum have a better opportunity of preparing for the rupture. The fact that an acutely obstructed gangrenous appendix usually lies free in the peritoneal cavity with little attempt by the omentum to surround it has been noted by many surgeons.

The foregoing discussion emphasizes the importance of realizing what occurs in acute appendicular obstruction and the value of distinguishing, when possible, between primary obstruction and primary inflammation. It explains the cases in which the patient remains under observation during several days of intermittent symptoms with normal temperature, pulse, and leucocyte count, and then acute, rapidly progressive appendicitis suddenly develops. The value of clinical suspicion lies in the early surgical intervention that it encourages.

One can appreciate, therefore, the importance of recognizing or suspecting this type of appendix in its early stage. If one waits until the signs of fever and leucocytosis appear, time is at a premium and immediate operation is urgent. It is like waiting for a strangulated hernia to become gangrenous.

#### SUMMARY

An attempt has been made to correlate the clinical and pathological picture seen in 70 cases in which operation was performed for an obstructive type of appendicitis. Gross examination of the organ usually provides sufficient evidence to classify a case of acute appendicitis as ob-

structive or nonobstructive. A characteristic microscopic picture confirms such evidence. Appendicular obstruction presents two phases in its development: the first, or early, phase is that of primary simple obstruction; the second, or late, phase begins when the supply of blood to the wall is impaired and bacteria invade the wall with resultant acute inflammation. The significance of the microscopic appearance of the early stage has been emphasized. Inasmuch as obstruction is one of the frequent factors in the production of appendicitis, the importance of its early recognition and treatment has been stressed.

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# THE SEX HORMONE EXCRETION OF ADULT FEMALE AND PREGNANT MONKEYS

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ALTHOUGH the monkey has been extensively employed for studies in reproduction, little is known of the normal metabolism of the steroid sex hormones in this species. Some work has been reported on the levels of the estrogenic and androgenic substances in the urine of the adult male and immature monkeys (5, 6, 7). This communication deals primarily with determinations of urinary estrogens and androgens in adult female and pregnant monkeys.

It has been found that if the fetus is removed some time between the seventieth and one hundred and fifty-seventh day of gestation, the placenta remains *in situ* and is expelled at the time when a living baby might have been delivered. From the gross appearances of generalized edema and intensification of the sex skin color, it appears that the animals maintain the habitus of pregnancy in spite of the absence of the fetus (11). We have studied the sex hormone excretion under these conditions to learn more of the endocrine state. We have included also in this report the study of a pregnant monkey in which the fetus was removed and the animal simultaneously bilaterally ovariectomized.

The results in this animal bring some direct evidence upon the rôle of the placenta and the adrenal cortex in the production of the steroid sex hormones.

## ANIMALS AND METHODS

Ten adult female rhesus monkeys (*Macaca mulatta*) were used in these experiments. For the studies on the concentrations of sex hormones in normal females, 6 animals were employed from which ten 3 day samples were quantitatively collected. A total of 4 normal pregnancies in animals A, B, and C were investigated, and at intervals of 2 weeks samples of urine were collected over a period of 3 days during each gestation. In addition, 4 other pregnancies were similarly studied in

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animals D, E, F, and G, in all of which, however, some form of operative intervention had been used. In 3 animals, D, E, and F, the fetus only was removed by abdominal hysterotomy at different intervals before term, but in animal G the ovaries also were excised when the fetus was taken out upon the seventieth day of gestation.

All urines were preserved with toluene during the periods of collection. The urinary concentrates were separated into the estrogenic and androgenic fractions, respectively, as previously described (8). The androgens were assayed by means of the day old chick method (4), at least 10 animals being used for each assay. All values for androgenic substances are expressed as international units (I. U.), which is that activity evoked by 0.1 milligram of androsterone. The estrogenic activity was assayed by means of the vaginal smear reaction in the spayed adult female mouse and all values for estrogenic material are expressed as international units (I.U.), which is that activity evoked by 0.1 microgram of estrone.

## RESULTS

The urinary excretion of androgenic and estrogenic substances by the adult female monkey is presented in Table I. No attempt was made to study the daily fluctuations of these androgens and estrogens, but rather to delimit the urinary concentrations of these substances. A total of 10 samples, each representing a composite of 3 days' urine, were collected from 6 different animals. The urinary content of estrogenic substances varied from 7 to 12 international units per 24 hours, while the concentration of androgenic substances varied from 1.2 to 3.6 international units per 24 hours with an average value of 2.2 international units.

Figure 1 illustrates the variations in the excretion of androgens and estrogens during 4 normal pregnancies in 3 monkeys (A, B, C). Definite increases in estrogenic substances are detectable between the thirtieth and sixtieth day of gestation. The highest value for estrogenic substances was found in monkey C at 114 days after conception when a value of 460 international units per day was determined. This represents a 46 fold increase above the nonpregnant levels for estro-

TABLE I.—THE SEX HORMONE EXCRETION IN THE URINE OF THE ADULT FEMALE MONKEY

Monkey	Days of cycle	Androgenic substances IU/24 hrs	Estrogenic substances IU/24 hrs
J	7, 8, 9	3.6	7
E	9, 10, 11	8.0	<10
C	11, 12, 13	1.8	9
H	11, 12, 13	2.0	<10
H	14, 15, 16	2.5	8
E	17, 18, 19	1.5	8
D	24, 25, 26	1.0	<10
J	25, 26, 27	2.5	12
C	27, 28, 29	2.7	<15
I	34, 35, 36	1.2	11

genic substances. Within 2 weeks after parturition the quantity of estrogens returned to normal nonpregnant levels.

1. Within the first half of the gestation period the androgenic substances showed a considerable increase over the normal nonpregnant values. In 3 of the 4 pregnancies studied values of androgenic material above 6 international units per day were recorded in comparison with the average value of 2.2 international units per day for the nonpregnant levels. In the fourth pregnancy the values for androgens were not as great as in the other 3 pregnancies, but still one value of 4.7 international units per day was recorded in contrast to the maximum value of 3.6 international units per day recorded for the normal adult females.

Within the first postpartum month the androgenic titer remained at a high level. Thus, in the case of monkey A between the thirteenth and sixteenth day the titer of androgenic substance was 4.0 international units, and between the twenty-seventh to thirtieth day, 5.0 international units. However, the concentration of androgenic substances returns to normal limits during the second postpartum month, as evidenced by the fact that in monkey A a value of 1.0 international units per day was found by the forty-eighth day after delivery.

The influence of the removal of the fetus on the urinary excretion of the sex hormones is presented in Figure 2. Three such cases were studied which included monkeys D, E, and F, from which the fetuses were removed by abdominal hysterotomy at the seventy-first, one hundred and forty-first, and one hundred and fifty-seventh day, respectively. The placentas were retained and finally expelled near the expected date of parturition.

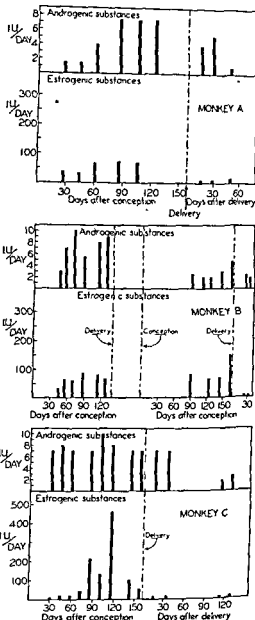


Fig 1 The urinary excretion of estrogenic and androgenic substances by the pregnant monkey

The removal of the fetuses caused no significant change in the urinary excretion of the sex hormones.

Figure 3 presents a study of the excretion of estrogens and androgens during a pregnancy in

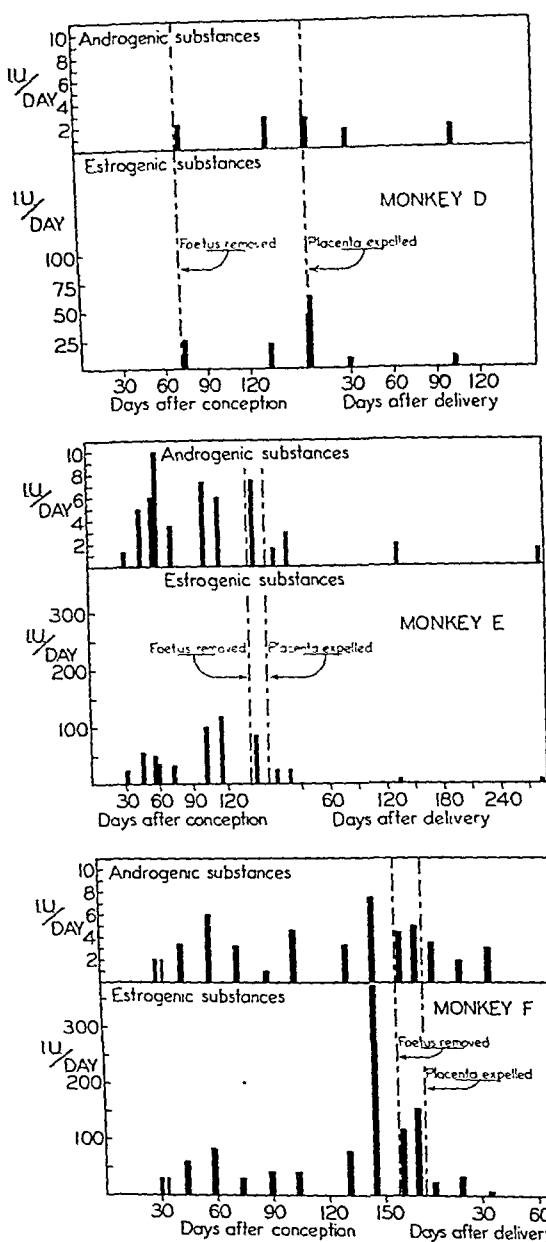


Fig. 2. The urinary excretion of estrogenic and androgenic substances by the pregnant monkey when the fetus was removed before term.

which animal G had been subjected to ovariectomy on the seventy-third day at the time of the removal of the fetus. The placenta was retained until the one hundred and fifty-third day, at

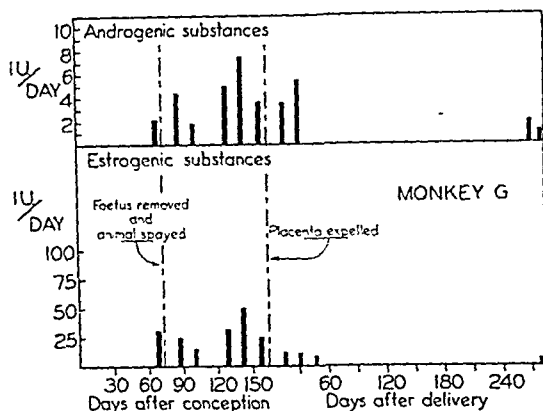


Fig. 3. The urinary excretion of estrogenic and androgenic substances by the pregnant monkey after removal of both ovaries and the fetus.

which time it was expelled. Throughout the period of placental retention the quantity of urinary estrogens was maintained well above the nonpregnant excretion figures of 7 to 12 international units, ranging from 15 to 50 international units per 24 hours. The androgen excretion during this same interval ranged from 1.8 to 7.5 international units per day with an average of 4.6 international units, and was definitely above the control values of 1.2 and 2.0 international units found about 6 months after the expulsion of the placenta. As in the case of normal pregnancy, the high titer of androgenic substances was maintained during the first postpartum month.

#### EVALUATION OF STUDY

The comparative urinary excretion of estrogenic and of androgenic substances in the monkey have been summarized in Table II. The immature animal excretes very little, if any, substance possessing estrogenic or androgenic activity. Both the adult male and female monkey, however, excrete measurable amounts of active substances. With respect to the estrogens, the female of this species seems to excrete considerably more than the male. The urinary excretion of androgenic substances is of interest since the quantity of these materials is of the same magnitude in both males and females, the average being 2.6 and 2.2 international units per day, respectively.

During pregnancy in the monkey we find increased concentrations as both estrogenic and androgenic substances in the urine; this, in the case of estrogens, may be as great as 46 times that of the normal female. The increase in estrogenic substances during pregnancy agrees with results found for the human (1).



TABLE II.—THE COMPARATIVE URINARY EXCRETION OF ESTROGENIC AND ANDROGENIC SUBSTANCES IN MONKEYS

References to literature	Sex of animal	Status of animal	Number of animals	Number of days' urine collected	Androgenic substances 1 U./Day (range)	Estrogenic substances 1 U./Day (range)
(5), (6)	♀	Immature	3	30	<0.05	<0.8
(5), (6)	♂	Immature	3	30	<0.05	<0.8
This report	♀	Adult	6	30	2.2	(7-11)
This report	♀	Pregnant	3	75	50* 2.5-10.0	83 10-460
(7)	♂	Adult	3	46	2.6 1.0-4.7	1 1.1-2.5

\*This is a minimum value since 10 of the 26 assays were minimum assays due to lack of extract

In keeping with previous observations in the monkey that the removal of the fetus does not interfere with the general status of pregnancy (11), we find that no significant change occurs in the excretion of estrogenic substances. When the pregnant animal was ovariectomized at the same time that the fetus was removed, the concentration of urinary estrogens was maintained well above the nonpregnant levels. The greater part of these estrogens was probably of placental origin because it was further noted that when the placenta was expelled the estrogen excretion definitely decreased. The source of the residual estrogens, that is, in the absence of both placenta and ovaries, was probably the adrenal cortex. The fact that the adrenal cortex can produce estrogens is well established, especially since estrone has been isolated from this source (2). Thus, it is apparent that three sources, the ovaries, the placenta, and the adrenal cortex, contribute to the production of estrogens during the period of pregnancy.

The presence of increased quantities of androgenic substances during pregnancy in the monkey is of considerable interest. The fact that this increase persists for about a month after the expulsion of the placenta in animals with or without ovaries indicates that the increased androgen production during pregnancy is due to the adrenal cortex. Hypertrophy of the adrenal cortex during pregnancy has been described in the human (10)

and in the guinea pig (9). The rhesus monkey is the first animal in which an increased quantity of urinary androgens has been demonstrated during pregnancy. Studies in humans have not indicated similar increases (3).

## SUMMARY

Studies have been made on the sex hormone excretion of (a) adult female monkeys, (b) pregnant monkeys, (c) pregnant monkeys from which the fetuses had been removed by abdominal hysterotomy, and (d) a pregnant monkey which was ovariectomized early in gestation when the fetus was removed.

Increases in both estrogenic and androgenic substances in the urine of pregnant monkeys were observed. Following parturition, or expulsion of the placenta alone, the estrogens immediately decrease to the nonpregnant values while the high concentration of androgens persists for approximately 1 month post partum. Direct proof is presented that the estrogens may be produced in the ovary, placenta, and adrenal cortex. The results indicate that the greatest part of the androgens produced during pregnancy are derived from the adrenal cortex.

The rhesus monkey is the first animal in which an increase in the urinary androgens has been demonstrated in pregnancy. The excretion of estrogenic and of androgenic substances is compared in immature, adult, and pregnant monkeys.

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## CECOSTOMY

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**T**HE importance of cecostomy in dealing with malignant lesions of the left colon has been recognized for many years. Recent advocates of this operation are Whipple and Rankin. Early procedures of this type were for relief of complete obstruction, and this is still the only use made of it by many surgeons, either as a palliative operation or as a preliminary procedure to resection. When obstruction of a marked degree does not exist, cecostomy is usually practiced as a complementary step in primary resection. On the whole, the application of these principles has given good results, particularly when the cases have been well selected and in the hands of certain surgeons. We believe our results (1) indicate that preliminary cecostomy, in all lesions of the left colon and in some cases of

carcinoma of the rectum followed by resection at a later stage, will result in a lower mortality rate than will cecostomy coincident with primary resection.

Our experience has been greater with resection and anastomosis of the bowel than with any of the various exteriorization or obstructive resection methods which are frequently used elsewhere. This probably explains our improved results in cases in which a preliminary cecostomy is performed 7 to 10 days prior to resection of the lesion, since leakage, peritonitis, or wound sepsis rarely follow resection and suture under these circumstances.

The earlier cecostomies consisted of exteriorization of the cecum and, in many instances, fixation of the bowel to the abdominal wall. This method is still widely used and when the vent is to be permanent, it is the procedure of choice. Many

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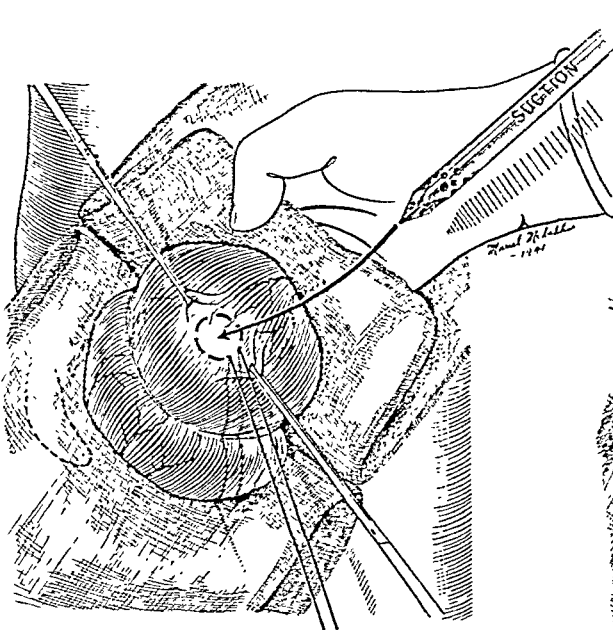


Fig. 1. The distended cecum has been delivered through a McBurney incision. The wound edges are carefully protected with gauze. A pursestring of No. 0 plain catgut has been placed, and suction trochar about to be introduced.

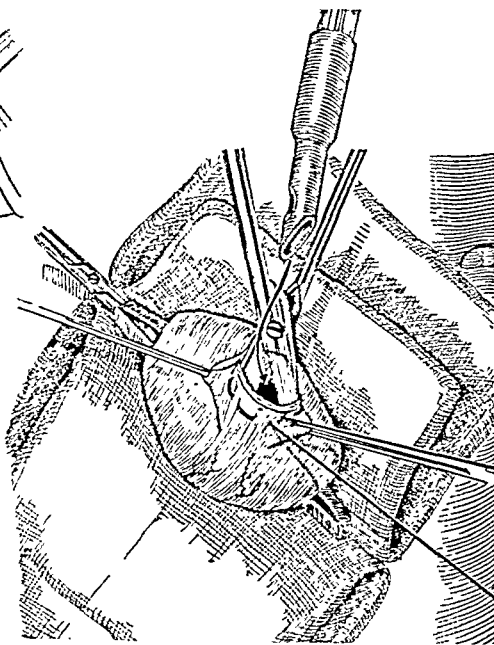


Fig. 2. The cecum has been decompressed and a rubber covered clamp applied. The cecum has been opened. As the scissors are spread, the rubber covering the right angle glass tube is inserted.

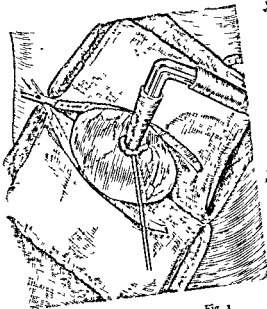


Fig 3

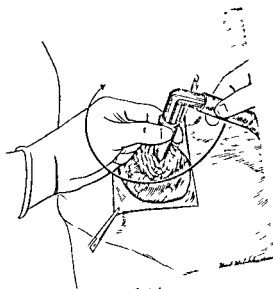
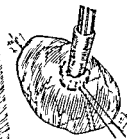
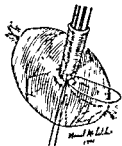


Fig 4

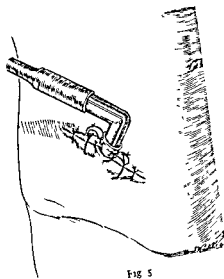


Fig 5

Fig 3 The pursestring is tightened and the same suture passed through the tube and tied. A second inverting pursestring of No. 0 chromic catgut is then placed.

Fig 4 A third pursestring of No. 0 chromic catgut has been inserted. The tip of the omentum has been sutured about the tube. The operator then holds the rubber tube

firmly and rotates the glass tube about until it reaches its final position.

Fig 5 The final appearance after wound closure. One through-and-through suture is tied on either side of the tube, and then passed through the rubber as an additional protection to maintain the position of the tube.

suggestions have been made for temporary cecostomy by the use of glass or rubber tubes of varying designs. When complementary cecostomy is to be established, the Pezzer catheter type of Hendon or Nason, with Nicholson's modification, is satisfactory. This method, however, has some disadvantages as a preliminary procedure. The glass tube method of Paul, or Mixer's (4, 7) modification of it, is also unsatisfactory since leakage about the tube occurs so soon after operation that control of the fecal current is quickly lost. Gibson advocated the use of a large rubber tube for cecal drainage in ulcerative colitis, and Jones used this method extensively in cecostomy as a preliminary and coincident procedure for carcinoma of the left colon.

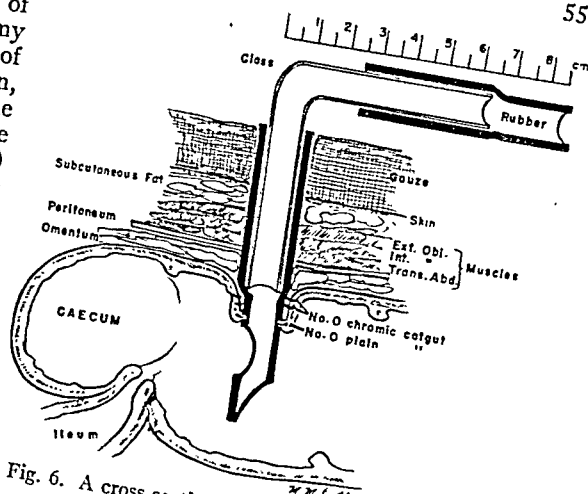


Fig. 6. A cross section of the tube in its final position.

(1) Wound sepsis invariably occurs to some extent and can be controlled by removal of sutures and warm boric acid solution compresses. Serious infection rarely, if ever, occurs and has caused no deaths in our series. (2) Hernia in scar is common, due to the long maintenance of the foreign body through the abdominal wall. Since it is necessary to keep the cecostomy open until the anastomosis is functioning well, this means that the tube remains in place for from 2 to 3 weeks. Usually these hernias cause little trouble and rarely do they warrant repair. (3) Failure of the cecostomy to close spontaneously occurs occasionally. It is wise to wait a minimum of 3 months and often complete cessation of drainage will take place long after that. Only when the mucous surface of the opening presents above the skin edges can one be sure that spontaneous closure will not take place, and this situation is rarely met if the procedure is carried out as we have described it. On the whole, the complications are a small price to pay for the numerous advantages of the procedure.

Our experience at the Massachusetts General Hospital with cecostomy, performed for malignant disease in a consecutive series of 250 cases ending January 1, 1941, is given in Table I.

TABLE I.  
Method

Method	Cases
Mixer's glass tube.....	22
Witzel.....	23
Pezzer catheter or exteriorization of cecum.....	11
Modified Gibson (as described by us).....	194
Total.....	250

We have found that a short segment of large rubber tubing, fitted on a right angle glass tube, gives the most uniform result in temporary cecostomy of any of the methods so far used. The rubber tubing holds well in the bowel wall and can be so placed by 3 pursestring sutures of catgut that the serous surfaces of the vent come in contact when the tube is removed, thus enhancing a spontaneous closure of the opening. The glass right angle tube, going through some or all of the abdominal wall, prevents kinking of the tubing, which is the chief disadvantage of any all rubber apparatus that we have tried. This rigid segment also makes it easier to fix the tube securely to the abdominal wall in such a manner that change of position can be accomplished by the patient with as little discomfort as possible. The bowel can usually be well cleansed by this procedure. After 24 hours, dilute magnesium sulphate can be instilled directly into the colon several times daily. Often salt solution can be irrigated through the lesion from the rectum to the cecostomy or vice versa. Occasionally, the bowel cannot be as thoroughly cleansed by this method as by complete colostomy and, for this reason, in large obstructed and grossly infected growths, one may do well to use transverse colostomy or Devine's modification of it either instead of, or, at times, following cecostomy before resection of the involved bowel is undertaken. It is well to bear in mind that the contents of the colon should be as dry as it is possible to make them at the time of resection, since liquid feces in small quantities are far more dangerous to the peritoneal cavity than firm scybala. For this reason, no irrigations of the colon should be made for 24 to 36 hours before resection, and, during this interval, paregoric in dram doses should be given every 4 hours.

The disadvantages of temporary cecostomy are:

There were 32 deaths in this series, 21 of which were due to perforated lesions or carcinomatosis. Eleven deaths were attributable to the cecostomy itself. In some instances, the fatality was due to an error in technique, in others to cardiac or pulmonary lesions.

Surgical closure of the cecostomy was necessary in 17 instances. There were 14 known recorded hernias in scar.

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# EDITORIALS

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## SURGERY Gynecology and Obstetrics

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OCTOBER, 1941

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### BRAZILIAN OPHTHALMOLOGY

I HAVE been requested by the Editorial Board of SURGERY, GYNECOLOGY AND OBSTETRICS to record my impressions of the practice of ophthalmology in Brazil after attending the IV biennial Brazilian Congress of Ophthalmology, held in Rio de Janeiro the last week of June of this year. Previously to that time, I knew one Brazilian ophthalmologist intimately and several others only very casually. I knew nothing of the methods or character of practice there. But I have come away with a very favorable impression.

The men from forty years of age upward were for the most part trained either directly or indirectly in the ophthalmic clinics of Central Europe, particularly Germany and Austria. But there is definite evidence that they thought for themselves and do not adhere slavishly to the fetishes of the individual clinic in which they spent the majority of their time. A few have supplemented their knowledge by visits of varying length of time in the clinical centers of the United States. French and

Italian influence, which formerly was in the ascendancy in Brazilian ophthalmic circles, has now entirely disappeared. The men of that generation are fairly conversant with the work being done in the United States, although the knowledge has been gained from the literature and seldom from personal contact.

Nearly all of the younger men have been trained in Brazil by serving as junior assistants in the university eye clinics of which there are eleven. The same disadvantage exists there as did until recently in the United States, namely lack of formalized instruction particularly in the basic sciences of ophthalmology. The instruction is mainly clinical and somewhat of the preceptorship type. However, instructional courses are beginning to make their appearance and without doubt, the adolescent period from which American ophthalmology is just emerging, will be considerably shortened in Brazil. In the tropics, things mature rapidly.

There is a much sharper differentiation between charity and private practice than we are accustomed to. Hospitals, as we know them, partly charitable, partly half-pay, and partly private, do not exist there. A hospital in Brazil is always a charitable institution regardless of whether it is supported by the national or state government, by religious orders, or by private agencies. Private patients are operated upon in sanatoria or what corresponds to the British nursing home. Some ophthalmologists with large practices maintain small hospitals of their own, of 2 to 15 beds, in conjunction with their consulting offices. The Army and Navy hospitals are excellent.

The ophthalmic equipment in the private offices and in the public institutions is good.

The older instruments were almost invariably German, but they are being replaced rapidly by modern American equipment. None of the optical instruments or glass is of local make.

The treatment of eye, ear, nose, and throat conditions is done by the same man only in the smaller communities, while in cities of from 35,000 upward, the men confine themselves to one or the other specialty. Long working hours are the rule. Usually the men work in the clinics or the hospitals in the morning and conduct their private practice in the afternoon from two to seven. Dinner is always at a late hour, and there are practically no evening hours of consultation. Men on duty in the Army and Navy hospitals are permitted to conduct private practice in the afternoons, as are many of the public health officers.

The individual practice of ophthalmology in Brazil is much as it is in the United States. We use the same instruments of diagnosis, the same nomenclature, and the same surgical procedures. Therapeutic measures vary but slightly. Refraction is more apt to be performed under mydriasis in the United States, while in Brazil, refractometers, either Bausch or Zeiss, are much favored. Anomalies of the ocular muscles have been more or less neglected in the past, but are now receiving greater recognition, due mainly to British influence. Some orthoptic training is being instituted, again principally of English origin. In certain parts of Brazil, tropical diseases bring ophthalmic problems that we do not have to cope with, but on the whole, individual ophthalmology in Brazil is on the same plane as in the United States.

Graduate training in ophthalmology is inadequate in Brazil, due principally to a lack of organization. The Congress that was just held, voted to establish a Brazilian Board of Ophthalmology, patterned much along the lines of the American Board of Ophthalmology.

That important decision will open the gate to ophthalmic organization, and because they can and will borrow from the experience of the American Board, progress will be more rapid in Brazil than it has been in the United States. There is a full realization there that ophthalmology for the future will be centered in the Americas, and the Brazilians are preparing to do their part.

HARRY S. GRADLE

## DIAGNOSIS, OPERABILITY OF INTRATHORACIC NEOPLASMS

**I**INTRATHORACIC neoplasms usually present first symptoms, physical signs, and occasionally even roentgenological shadows that strongly suggest some commonplace thoracic disease. The great majority of thoracic neoplasm patients are first diagnosed as having a simple cold, influenza, pneumonia or delayed resolution of pneumonia, tuberculosis, asthma, pleurisy with effusion, chronic bronchitis, bronchiectasis, pulmonary abscess, various forms of cardiocirculatory disease, diaphragmatic hernia, arthritis, neuralgia, or miscellaneous other conditions. The diagnostic error is prolonged if the physician fails to become concerned by the persistence of symptoms in what he had diagnosed as a self-limited disease, or by the atypical course of some presumed chronic disease. The persistence or aggravation of the significant symptoms of cough, dyspnea, and pain should lead to a re-evaluation of the clinical findings, especially the roentgenological findings. While the mistaking of a non-neoplastic lesion for a neoplasm occasionally occurs and may lead to an unnecessary operation, the opposite mistake is much more frequently made.

There is a rather generalized belief among physicians that, once a diagnosis of neoplasm has been made, immediate surgical removal is required only for those tumors believed to be

malignant. Consequently, tumors that are believed to be benign, but that are actually malignant, are often merely observed until such time as their malignant nature becomes manifest; in many cases the lesion becomes inoperable during the period of observation. There are, furthermore, real dangers in merely observing neoplasms that are actually benign when first diagnosed, as the continued enlargement of a benign tumor produces various forms of progressive disfunction of the lungs, heart, and other mediastinal organs, and as the contents of a cystic tumor, or the liquefied degenerated portion of a solid tumor, may perforate into a bronchus; the most important danger, however, is that benign neoplasms not rarely undergo malignant degeneration.

Since benign as well as malignant neoplasms should be removed promptly, the clinician's chief concern should be to determine whether a given tumor is probably completely removable and whether the patient's general condition will permit the intended operation. The operative risk should obviously be weighed against the probable malignancy or benignancy of the tumor; when the risk is sufficiently great that it would be accepted only if the tumor were malignant, a needle punch biopsy of the lesion is justifiable. A careful search should be made for evidence of metastasis or irremovable invasion of the thoracic walls. Bronchoscopy will determine whether a bronchogenic carcinoma has extended too far cephalad to be completely removed by total pneumonectomy. A tumor, especially one of the mediastinum, that might be a lymphoblastoma should be given a diagnostic test dose of deep x-ray therapy. This use of x-ray therapy is its only proper one for possibly operable intrathoracic neoplasms.

The rapid rate of growth of a tumor suggests malignancy but is not conclusive evidence since some benign tumors grow rapidly and

some increase rapidly in size from hemorrhage into, or rapid increase in the liquid contents of, a cystic tumor. Furthermore, some malignant neoplasms grow very slowly and may metastasize while the original lesion is still small. Most intrapulmonary neoplasms are malignant, being carcinomas, and may be either well or poorly circumscribed, roentgenologically. Although most extrapulmonary neoplasms with well circumscribed borders are benign and those with poorly defined borders are malignant, the former are occasionally malignant and the latter benign. While the following signs are strongly suggestive of malignancy, all have occurred in cases of benign tumor: Paralysis of the phrenic, recurrent laryngeal and upper thoracic sympathetic nerves, dysphagia, dilatation of superficial veins, hemorrhagic pleural effusion, serous pleural effusion in the presence of a small neoplasm, great pain, and great loss of weight.

Since delay in removal of malignant neoplasms is not justifiable and since delay in removal of benign neoplasms exposes the patient to certain considerable risks, virtually all presumably removable intrathoracic neoplasms (with the exception of lymphoblastomas) should be operated upon soon after the diagnosis has been made, provided, of course, that the patient's general condition permits. The importance of early operation is increased by the facts that in many cases an accurate determination of malignancy or benignancy cannot be made before operation and that delay in operating in the case of those tumors that happen to be malignant often results in their becoming inoperable. Early surgery for almost all intrathoracic neoplasms will prevent many tragic deaths that would occur as a direct result of the postponement of operation in the usually unfulfilled hope that a preoperative pathological diagnosis might, somehow, soon be made.

JOHN ALEXANDER.





# TEXTS AND DOCUMENTS

## ON THE DIPLOMA AND CEREMONIES INCIDENT TO THE AWARD OF THE MEDICAL DEGREE AT BOLOGNA, ITALY, IN 1698

BLANCHE B. BOYER, and ARNO B. LUCKHARDT, M.D., Chicago, Illinois

THE modern *cap* and *gown*, official dress, at present day University convocations are, of course, curious modifications of the monastic "cowl" and "cuculla" not uncommon to this day in various materials and colors depending on the particular monastic or religious order. In the religious orders the hood or cowl is usually attached to the monk's scapular. The present day hood placed over the head and about the neck and shoulders of the present day recipient of an earned or honorary degree is a curious and misshapen homologue of the cowl attached to the scapular of which latter there is no vestigial remnant in the modern academic gown. Because of this, there was evolved in the course of time at the English speaking universities the "headgear" spoken of as the "mortarboard" or "cap" quite different from the birretum and from the earlier monk's cowl which still constitutes a serviceable protective covering for the head.

As in the case of dress, so the ceremonies incident to the investiture of a candidate on graduation have been greatly modified in the course of time, as is very evident from the diploma of the M.D. and Ph.D. degree awarded to one Franciscus Ignatius of Ravenna by the University of Bologna in 1698.

Senior author, Miss Blanche Boyer, translated from the Latin *in toto* the text of this diploma. Only such passages will be reproduced in translation as are of interest because of their novelty. The document belonging to the junior author consists of a book measuring  $8\frac{1}{2}$  inches by  $6\frac{1}{2}$  inches, bound in full calf and containing one hand colored frontispiece and four pages of text, hand printed on parchment.

Dr. Boyer, Assistant Professor of Latin, The University of Chicago (Paleographer).

In the frontispiece (Fig. 1), on the left is seated the figure of Minerva, goddess of wisdom, arts, and crafts, to whose usual attributes is added the caduceus. With the left hand she proffers the flower of learning to Bologna (the seated figure on the right, identified by the coat of arms—red cross on white background, surmounted by three gold stars—inscribed *Liberty*). Bologna with her right hand to a star in the upper center of the picture says, "If it be filled with dew" ("the flower will thrive" by context). Across the bottom of the picture runs the legend:—"Forever will live . . . good from me." The last page of the Latin text ends with the following transcription (Fig. 2) in translation:

"I, Antonius Felix Marsilius, Archdeacon and Senior Chancellor of the University of Bologna, testify to the acceptance of D. (ominus) Franciscus Ignatius of Ravenna in the aforesaid Faculties of Doctors. . . .

"I, Dominicus Maria, son of D. Angelus of Jordani, Notary authorized by the Holy See, the Empire and the City of Bologna, and special secretary of His Grace and Very Reverend Lord the Archdeacon, since I was present at the foregoing request of the aforesaid eminent D. Franciscus Ignatius admitted with no dissenting vote into the aforesaid Faculties of Doctors, have therefore subscribed with my own hand to all the foregoing—drawn in the form of a public document by another's trustworthy hand—and have stamped it as required. Dated: Bologna, 24th of September, 1698."

The document commences with exuberant praise and flattery of the officials of Bologna and its university, so common to that age and hardly of interest to this journal's readers.

Next the document refers in glowing terms to the doctoral candidate, "D. Mv. Franciscus Ig-

natus, most eminent citizen of Ravenna" who "has undergone a difficult, rigorous and formidable examination by the Domini D. D. Doctors of said college of Liberal Arts, Sacred Philosophy and Medicine in Bologna in which said eminent D. Mr. or Dominus Franciscus Ignatius" expounded so cleverly "with unusual clarity the topics given him, by shrewd argument and clever answer after the fashion of Doctor rather than Scholar" that he was adjudged fit and satisfactory by "unanimous vote with no dissenting sign" to be "candidate for the Degree in the aforesaid Faculties."

It was also determined that his faith was beyond suspicion, for after a "prefatory discourse and information duly and rightfully received regarding the religion and Catholic faith of said eminent D. Franciscus Ignatius by the summoning and examining of reliable witnesses and by public avowal of the candidate with the oath of the Catholic faith in the usual set formula pre-

scribed in the Bulla and Apostolic letters of Pope Pius IV of blessed memory" etc.

Everything having been found satisfactory and the candidate having requested *the insignia of the Doctorate* the procedure was as follows:

"Books of the Liberal Arts and sacred Philosophy and Medicine closed were placed in his hands, then, the same open, second, the birretum or Doctoral cap was put on his head; third, he was pledged in the name of all branches of learning with a ring of gold; then the kiss of peace and the Magisterial benediction that the same eminent D. Franciscus Ignatius, Distinguished Doctor, should be thus decorated and conspicuously rewarded in his Fatherland by Him who One and Three reigns unnumbered centuries, eternal and glorious."

Surely a most ceremonious and time consuming procedure for *one* doctor compared with the hurried and perfunctory "mass production" practice at convocations of the present time.

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

IN the splendidly written book *Clinical Roentgenology of the Alimentary Tract*<sup>1</sup> Buckstein has drawn liberally not only from the literature but particularly from his rich experience in the field of gastroenterology. In the preface and throughout the text the importance of the correlation of the clinical, etiological, and pathological with the roentgenological aspects of diseases of the alimentary tract is stressed. Since roentgenography has become such an essential procedure in the diagnosis of lesions of the alimentary tract, it is important that any physician having to deal with the diagnosis and treatment of such lesions have a knowledge of the potentiality of this method. In many instances the diagnosis will be evident on the roentgenogram but not infrequently in the borderline cases only a correlation of the clinical and the roentgen findings will lead to a correct interpretation.

This volume includes not only an excellent presentation of the roentgenology of the digestive tube, the biliary tract, the spleen, liver, and pancreas, but also pertinent details as to roentgenographical technique and procedures so important in an adequate examination. The importance of using both fluoroscopy and radiographical methods are discussed and emphasized. There should be no controversy as to which method is most important as both are essential for an adequate and complete examination of the alimentary tract. Throughout the volume the author has presented numerous interesting case reports which help to emphasize the roentgen findings. The illustrations are numerous, well chosen, and beautifully reproduced, and add greatly to the clarity of the discussion.

This comprehensive, easily readable, and dependable volume should prove most helpful and instructive, not only to the roentgenologist and gastroenterologist but to the physician in general practice whose needs the author has kept in mind throughout the presentation. It is recommended without reservation and merits wide distribution.

EARL E. BARTH.

THE volume by Dr. Salter<sup>2</sup> contains an authoritative presentation of present day knowledge of iodine in physiology and biochemistry. The text includes the author's very extensive work in this field so that it is a most valuable monograph. In addition, it gives a review of physiological and chemical literature on iodine. More than 600 references are listed.

<sup>1</sup>CLINICAL ROENTGENOLOGY OF THE ALIMENTARY TRACT. By Jacob Buckstein, M.D., Philadelphia and London: W. B. Saunders Co., 1919.  
<sup>2</sup>THE ENDOCRINE FUNCTION OF IODINE. By William Thomas Salter. Cambridge, Massachusetts: Harvard University Press, 1942.

Of necessity, thyroid gland physiology is thoroughly discussed, so that, as the preface indicates, "an important bridge between biochemistry and endocrinology" is provided. Recent studies of radioactive iodine as a means of elucidating iodine metabolism are discussed. Blood iodine and iodine balance studies in various thyroid diseases are presented and much of the modern data are reproduced in tabular and graphic form. Iodine metabolism in other diseases and physiological states is also reviewed. The technique of iodine determination in biological material is given in detail. Hence, this volume is essential to students of clinical endocrinology as well as to biochemists. It cannot be recommended too highly.

PAUL STARR.

THE eighth edition of *Williams Obstetrics*<sup>3</sup> has recently been made by Stander, this being his second revision of the well known text. The book has been almost completely rewritten and little of the original text remains unaltered. Three new chapters have been added: "Diseases and Abnormalities of the Newly Born Child," "Classification of Abnormal and Contracted Pelves," and "Sudden Death and Maternal Mortality." This text has been accepted as a classic for so long that an extended review is unnecessary. The field of obstetrics has been completely covered, and all recent advancements made in the field are incorporated in the text. Controversial theories and different teachings are presented, and the author's own views and teachings are definitely stated.

In the chapter on classification of abnormal and contracted pelvis, Stander presents the modified Williams classification, which is based on an etiological basis. The morphological classification of Caldwell and Moloy based on sexual and anthropological characteristics is presented, as is also the Thoms classification of pelvis. A new classification of contracted and abnormal pelvis is proposed by Stander; this classification is based on a combined morphological and etiological classification and is arranged on a basis of inherited, sexual, developmental, growth, disease, and traumatic factors. Roentgenological pelvimetry is discussed in detail and techniques of the procedure are also described in full detail.

In the new chapter, diseases and abnormalities of the newborn child, abnormalities, injuries, and diseases occurring during pregnancy, labor, and shortly thereafter are discussed.

<sup>3</sup>WILLIAMS OBSTETRICS. By Henricus J. Stander, M.D., F.A.C.S. 8th ed. New York and London: D. Appleton-Century Co., 1941.

The chapter on the toxemias of pregnancy has been revised, and the toxemias are classified and discussed according to the new classification of the American Committee on Maternal Health. Hypertensive disease and renal disease complicating pregnancy, while not true toxemias of pregnancy, are discussed in this chapter because of their similarity in several respects to the toxemias. Clinical and laboratory methods of diagnosis and differentiation of this important group are given in detail, and their treatment, in view of our present knowledge of these conditions, is thoroughly presented.

The chapters on operative obstetrics are most complete and operative procedures are well visualized by means of photographs and drawings. The chapter on amnesia, analgesia, and anesthesia gives the history and progress of the preparation used from their inception to the present. Their methods of use, advantages, and disadvantages are fully stated and details of application employed at present in the New York Lying-In Hospital are outlined.

This is a most valuable book for students and practitioners, and essential to the library of anyone teaching obstetrics.

THEODORE J. MORRIS.

WELL known for his contributions to the knowledge of blood coagulation, Dr. Nygard has recently written *Hemorrhagic Diseases*. Much of the present work centers around the method developed by a photo-electric method of determining the coagulability by a photo-electric method is the measure of light transmission through recalcified blood plasma during fibrin formation. Automatic graphic recordings are made of the progressive reaction. From the curves, it is possible to determine the time of the first formation of fibrin, the duration and velocity of fibrin formation and the appearance of retraction of the clot. This method obviously gives much more accurate and detailed information than clinical methods for blood coagulation now in use.

In the first part of the book, the writer outlines the methods of determining coagulability of the blood and describes in detail the principles of the photo-electric method. In part II are included experimental investigations on the coagulability of blood plasma, the interaction of thrombin and fibrinogen and the coagulant effect of thromboplastin. The photo-electric method helps greatly to clarify the mechanism of blood coagulation. In the last part of the book there is a complete classification of "hemorrhagic manifestations." The comprehensive chapters on hemophilia, thrombocytopenic purpura, vitamin K, jaundice, and hemorrhagic disease of the newborn include many interesting and original observations on the coagulation defect in these conditions.

More complicated sections of the book are simplified by many well chosen illustrations and tables.

Complete references are given at the end of each chapter. This excellent volume should be of great value to both physiologists and clinicians interested in the problem of blood coagulation.

HOWARD L. ALT.

ACCORDING to its preface, *Spermatozoa and Sterility* by Abner I. Weisman<sup>1</sup> is an effort to bring to the attention of those interested in sterility the tremendous importance of semen, spermatozoa, and spermiation in the female by concentrating in one volume all of the available information on the subject up to the present time. In this effort, Dr. Weisman has very largely succeeded.

Seventeen of the book's 27 chapters have to do with the seminal fluid or its constituents. The chemistry, metabolism, and reaction of spermatozoa to external stimuli are adequately discussed. Methods for obtaining and evaluating spermatozoa are given in excellent detail. Specific instructions for collecting and counting spermatozoa, and for studying spermatozoal morphology are presented in a simple, lucid manner. In a discussion of the interpretation and evaluation of seminal analysis the author correctly directs attention to the fact that a single seminal specimen does not, in itself, give a complete picture of the human male's procreative ability. Thorough physical examination and repeated study of the seminal fluid are essential. While the value of many of the procedures included as auxiliary tests of spermatozoal function would be questioned by some gynecologists, yet they are rightfully included in a comprehensive compilation of the literature.

The problem of artificial impregnation with either the husband's or a donor's semen is presented not only from the medical but also from the legal aspect. The pitfalls inherent in such unnatural procedures are pointed out and measures directed toward decreasing some of the dangers associated with artificial insemination are given. Special chapters are devoted to pregnancy tests, spermatoxins, control of sex, and theoretical factors in fertility and sterility. Only two rather brief chapters deal in a general way with the causes of sterility in the male and with the treatment of impaired spermatogenesis.

The text is an excellent source book not only for the gynecologist and the urologist but also for the experimental laboratory worker as well. It is somewhat voluminous to be considered an ideal manual for the general practitioner. The text contains references to and excerpts from most of the authoritative investigations of human sterility. The monumental work of Retzius has been emphasized but it is to be regretted that Gatenby's and Beans' newer observations on spermatozoal morphology were overlooked. Throughout the text the author has been meticulous in giving credit for original work. His book is a timely reminder of the need for a careful study of the husband's seminal fluid in human sterility problems.

JOHN W. HUFFMAN

<sup>1</sup>SPERMATOZOA AND STERILITY, A CLINICAL MANUAL. By Abner I. Weisman, M.D. New York and London: Paul B. Hoeber, Inc., 1941.

*HEMORRHAGIC DISEASES. PHOTO-ELECTRIC STUDY OF BLOOD COAGULATION.* By KARL A. NYGARD, M.D. St. Louis, Mo. The C. V. Mosby Co. 1941.

# CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

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## PROGRAM FOR THE 1941 CLINICAL CONGRESS IN BOSTON

THE fellows of Boston and vicinity will sponsor the thirty-first annual Clinical Congress of the American College of Surgeons November 3 to 7, when the facilities of that great medical center will be employed to provide a clinical program of exceptional interest. The co-operation of Boston's three medical schools and some 30 approved hospitals is assured. Operative clinics and demonstrations in the hospitals will cover many phases of general surgery and the surgical specialties. Leaders of the profession from many sections of the country will participate in the panel discussions and other scientific meetings at the headquarters hotels. The Hospital Standardization Conference will attract visitors of outstanding reputation in the hospital field. The program will be one of broad scope and interest, and it may be confidently expected that the notable contributions to medicine and surgery made at previous meetings in Boston, beginning in 1915, will be repeated.

### CLINICAL PROGRAM

The clinical program for the five-day meeting is being arranged under the leadership of a strong and representative Committee on Arrangements. An extensive schedule of clinics, symposia, and demonstrations in the hospitals and medical schools will, as usual, be the major feature of the Congress. Visiting surgeons will be given opportunity to observe and obtain first-hand information on a wide variety of surgical and related subjects, in the favorable environment of excellent hospital facilities. In the operative clinics, surgical technique, use of operating room equipment, and organization of personnel will be demonstrated. The symposia and non-operative clinics will deal with the broader but equally im-

portant aspects of diagnosis, related medical treatment, pre-operative preparation and post-operative care. The discussions will be augmented by the presentation of clinical material. Diagnostic methods will be demonstrated by various hospital departments. Specialists in many other fields will participate in the clinical program at the hospitals in order that the subjects may receive consideration from different viewpoints. The preliminary clinical program appearing in the following pages is to be revised and amplified in the weeks preceding the Congress.

The medical schools and their affiliated hospitals have developed a series of exhibits presenting their work in clinical investigation and the latest advances in surgical research. These exhibits will be available for study in the local hospitals during the entire meeting. Basic science departments of the medical schools will contribute to the program by arranging exhibits and demonstrations related to surgical practice. Thus the Boston institutions have much to offer in the way of a highly concentrated postgraduate course in surgery and allied subjects.

The clinical program is so arranged that the visiting surgeon may readily select the clinics which he wishes to attend. The schedule for each hospital will cover subjects in general surgery, obstetrics and gynecology, fractures, orthopedic surgery, thoracic surgery, neurosurgery, genitourinary surgery, ophthalmology, otorhinolaryngology. Presentation of subjects under these classifications is so correlated that he will have the opportunity to devote his time continuously to clinics dealing with the specialty in which he is most interested. The clinical program as published daily will be arranged according to these classifications. Each afternoon during the Congress, the

## CLINICAL CONGRESS PROGRAM IN BRIEF

*Monday, November 3*

- 9 30 Film Exhibition, General Surgery, Statler
- 10 00 Film Exhibition, Eye, Ear, Nose and Throat Surgery, Statler
- 10 00 Hospital Conference, Copley-Plaza
- 1 30 Panel Discussions (4), Statler
- 2 00 Film Exhibition, General Surgery, Statler.
- 2 00 Clinics in Boston Hospitals
- 2 00 Hospital Conference, Copley-Plaza.
- 3 00 Assembly of Initiates, Reception, Hancock Hall.
- 3 30 Panel Discussions (4), Statler
- 8 00 Presidential Meeting and Convocation, Symphony Hall.

*Tuesday, November 4*

- 7 45 Breakfast Conference, Copley-Plaza
- 9 00 Clinics in Boston Hospitals.
- 9 00 Film Exhibition, Eye, Ear, Nose and Throat Surgery, Statler.
- 9 30 Hospital Conferences (2), Copley Plaza
- 9 30 Forum on Fundamental Surgical Problems, Copley-Plaza.
- 11 00 Hospital Conferences (2), Copley-Plaza.
- 11 00 Group Conferences, Eye, Ear, Nose and Throat Surgery (2), Statler
- 12 00 Film Exhibition, General Surgery, Statler
- 1 30 Panel Discussions (3), Statler
- 2 00 Clinics in Boston Hospitals
- 2 00 Hospital Conference, Copley-Plaza
- 2 00 Cancer Symposium, Copley-Plaza
- 3 30 Panel Discussions (4), Statler
- 5 15 Clinical Pathological Conference, Statler
- 6 00 Film Exhibition, General Surgery, Copley-Plaza
- 7 00 Film Exhibition, Eye, Ear, Nose and Throat Surgery, Statler
- 8 00 Hospital Conference, Copley Plaza
- 8 00 Scientific Session, General Surgery, Copley Plaza
- 8 00 Scientific Session, Ophthalmology, Statler
- 8 00 Scientific Session, Otorhinolaryngology, Statler

*Wednesday, November 5*

- 7 45 Breakfast Conference, Copley-Plaza
- 9 00 Clinics in Boston Hospitals
- 9 00 Film Exhibition, Eye, Ear, Nose and Throat Surgery, Statler
- 9 30 Hospital Conference, Copley Plaza
- 9 30 Forum on Fundamental Surgical Problems, Copley Plaza
- 9 30 State and Provincial Judiciary Committees, Hancock Hall
- 10 00 State and Provincial Executive Committees, Hancock Hall.
- 10 30 State and Provincial Credentials Committees and Committees on Applicants, Hancock Hall.
- 11 00 Group Conferences, Eye, Ear, Nose and Throat Surgery (2), Statler
- 12 00 Film Exhibition, General Surgery, Statler

- 12 00 Meeting of Board of Governors, Copley Plaza
- 1 30 Panel Discussions (4), Statler
- 2 00 Clinics in Boston Hospitals
- 2 00 Symposium on Fractures and Other Traumas, Copley-Plaza
- 2 30 Hospital Conference, Demonstrations in local hospitals
- 2 30 Film Exhibition, General Surgery, Statler
- 3 30 Panel Discussions (4), Statler
- 5 15 Clinical Pathological Conference, Statler
- 6 00 Film Exhibition, General Surgery, Copley Plaza
- 7 00 Film Exhibition, Eye, Ear, Nose and Throat Surgery, Statler
- 8 00 Scientific Session, General Surgery, Copley Plaza
- 8 00 Joint Session, Sections on Ophthalmology and Otorhinolaryngology, Statler.
- 8 00 Hospital Conference, Motion Pictures, Copley-Plaza

*Thursday, November 6*

- 7 45 Breakfast Conference, Copley Plaza
- 9 00 Clinics in Boston Hospitals
- 9 00 Film Exhibition, Eye, Ear, Nose and Throat Surgery, Statler.
- 9 30 Forum on Fundamental Surgical Problems, Copley Plaza
- 9 30 Hospital Conference, Copley Plaza
- 11 00 Hospital Conference, Copley Plaza
- 11 00 Group Conferences, Eye, Ear, Nose and Throat Surgery (2), Statler
- 12 00 Film Exhibition, General Surgery, Statler
- 1 30 Annual Meeting of Governors and Fellows, Copley-Plaza.
- 2 00 Clinics in Boston Hospitals
- 2 00 Hospital Conference, Copley-Plaza
- 3 30 Panel Discussions (5), Statler
- 3 30 National and Regional Fracture Committee, Copley Plaza.
- 5 15 Clinical Pathological Conference, Statler
- 6 00 Film Exhibition, General Surgery, Copley Plaza
- 7 00 Film Exhibition, Eye, Ear, Nose and Throat, Statler
- 8 00 Scientific Session, General Surgery, Copley Plaza
- 8 00 Scientific Session, Ophthalmology, Statler
- 8 00 Scientific Session, Otorhinolaryngology, Statler

*Friday, November 7*

- 9 00 Clinics in Boston Hospitals
- 9 30 Film Exhibition, Eye, Ear, Nose and Throat Surgery, Statler
- 9 30 Film Exhibition, General Surgery, Statler
- 9 30 Forum on Fundamental Surgical Problems, Copley Plaza
- 1 30 Panel Discussions (4), Statler
- 2 00 Clinics in Boston Hospitals
- 2 00 Film Exhibition, General Surgery, Statler
- 3 30 Panel Discussions (3), Statler
- 8 00 Boston Surgical Society, John Hancock Hall

complete detailed clinical program for the succeeding day will be posted in the form of bulletins at headquarters in the Statler Hotel. On the following morning this final program will be distributed in printed form. As much information as it is possible to obtain in advance is being published in the preliminary programs and the general program, but it is necessary that those who attend

the Congress make their clinic ticket selections from the daily bulletins. This will facilitate proper selections and distribution of clinic tickets.

## PRESIDENTIAL MEETING AND CONVOCATION

On Monday evening in Symphony Hall, the combined Presidential Meeting and Convocation will be opened by an impressive processional of

the officers, regents, and honorary guests. Welcome will be extended to the assembly by the chairman of the local Committee on Arrangements, Dr. Leland S. McKittrick. Honorary guests will then be introduced, following which Dr. Everts A. Graham, the retiring president, will deliver the presidential address. Other events on the program of this meeting will be the inaugural ceremony for the incoming officers, the presentation of the initiates for fellowship, and the awarding of the Medical Records Prize.

#### SCIENTIFIC SESSIONS

The scientific meetings, to be held on Tuesday, Wednesday, and Thursday evenings in the ballroom of the Copley-Plaza Hotel, will be addressed by surgeons and specialists recognized as authorities in their respective fields. Complete programs for all scientific sessions will be found in the following pages. The annual oration on surgery will be given by Dr. W. Edward Gallie, Toronto, Ontario, on Tuesday evening.

The Board of Regents of the College has given careful attention to the selection of speakers and subjects for these evening sessions so that a well-rounded program introducing the newer developments in general surgery and the surgical specialties may be assured.

Great interest has been demonstrated during recent years, at both the Clinical Congress and sectional meetings of the College, in the panel discussions held at headquarters each afternoon. For the Boston meeting a schedule of thirty-five of these sessions has been planned for Monday, Tuesday, Wednesday, Thursday, and Friday. Recognized authorities in the fields under discussion will lead these panels, and with the aid of collaborators especially qualified will present the fundamental facts and direct the discussions in such a way that different viewpoints may be expressed. These sessions afford an opportunity for a larger number of surgeons to participate in the discussions and learn of the ideas and experiences of others. A ten-minute presentation of the subject is made by the leader, followed by brief remarks by the collaborators on various phases of the topic. As the major feature of each session, general discussion from the floor will be encouraged. This type of program will permit more informal discussion than usually takes place in larger general meetings. The subjects of the panels are carefully selected in order to cover many pertinent problems in various fields of surgery. It is suggested that surgeons who have questions which they would like to have considered in any panel discussions they plan to attend, should commu-

nicate in advance with the panel leaders so that if possible such questions may be specially incorporated in the program. This will help to assure discussion of points which those in attendance would like to have clarified.

Important features of the afternoon meetings at the headquarters hotels are a symposium on "Cancer" on Tuesday and one on "Fractures and Other Traumas" on Wednesday. It should be noted also that special panel discussions deal with "The Organization and Conduct of Cancer Clinics in Hospitals," and "Graduate Training in Surgery." Because of the wide interest in these subjects, it is expected that these meetings will attract a large attendance.

In formulating the program it is the aim of the Board of Regents and the committee to make it possible for each surgeon to learn of the newer developments in his field of practice. The subjects presented in the hospital clinics, panel discussions, and other scientific meetings will appeal to the surgical specialist as well as to the general surgeon. Each feature of the meeting has been carefully planned with this idea in mind. The detailed programs for these sessions will be found on the following pages.

#### FORUM ON FUNDAMENTAL SURGICAL PROBLEMS

A new feature to be introduced at the Clinical Congress in Boston is a "Forum on Fundamental Surgical Problems," the plans for which have been formulated by a committee under the chairmanship of Dr. Owen H. Wangenstein, of Minneapolis. In authorizing this new program it is the purpose of the Board of Regents to enable younger men representing various university departments of surgery to present the important results of their clinical and experimental research work before one of the larger surgical meetings. Heretofore, there has been limited opportunity for the younger men, many of whom have not yet qualified for membership in the principal surgical societies, to present their original work and ideas before representative surgical bodies. As surgery is concerned today not only with anatomy and pathology but to a growing extent with physiology, chemistry and physics, it is felt that the Clinical Congress program will be further broadened by the presentation of the best of this material and that surgeons attending the Congress may distinctly benefit therefrom.

Sessions will be held on Tuesday, Wednesday, Thursday and Friday mornings in the ballroom of the Copley-Plaza Hotel with presentations of original and experimental work related to general surgery and the surgical specialties. There will be



## SURGERY, GYNECOLOGY AND OBSTETRICS

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no prepared discussions but opportunity will be afforded those who attend to ask questions. Presentations will be limited to ten minutes each. It is expected that some of the best examples in surgery and highly constructive developments in surgery will be presented, and there is every indication that a live and active surgical forum in which younger men may participate will constitute one of the most important activities of the Congress in the future.

The committee in charge has been highly pleased with the response to this idea. Over 125 abstracts of subjects available for presentation have been submitted, and from this material the committee will select the most outstanding for the forum. The subjects, together with brief abstracts, will be published in the final program of the Clinical Congress.

### OPHTHALMOLOGY AND OTORHINOLARYNGOLOGY

The Congress will include an extensive program of scientific sessions and clinical demonstrations for ophthalmologists and otorhinolaryngologists. Separate sessions scheduled for Tuesday and Thursday evenings will include papers and symposia on pertinent subjects in these fields. The leaders will direct the discussions in the meetings so as to cover many phases of a general subject in each of the specialties. Those attending will have an opportunity to express their viewpoints. On Wednesday evening, there will be a joint meeting of ophthalmologists and otorhinolaryngologists with a symposium on "Neurosurgery as Related to the Eye and Ear." This type of program promises to attract wider interest than the presentation of formal papers.

Clinics in the Boston hospitals each morning and afternoon for the visiting ophthalmologists and otorhinolaryngologists will demonstrate surgical work of great variety. On Tuesday, Wednesday, and Thursday mornings, in addition to the hospital program, there will be clinical conferences for each group of specialists at the Statler Hotel. These are being arranged so that the leader will briefly survey the field for discussion in a ten-minute period. The larger meeting will then be broken up into small groups, limited to 20, and under separate leaders where there will be an opportunity for everyone to ask questions and participate in the discussion. Each visitor will select in advance the smaller group which he wishes to attend. In this manner, the general subject may be reviewed thoroughly and each visitor will benefit by the experiences and ideas of his colleagues. The morning and evening meetings will be preceded by the showing of selected motion

picture films on subjects related to ophthalmology and otorhinolaryngology. The detailed programs of these special meetings appear in the following pages.

### SPECIAL MEETING OF BOSTON SURGICAL SOCIETY

On the evening of Friday, November 7, in John Hancock Hall, which is located midway between the Statler and Copley-Plaza Hotels, the Boston Surgical Society will hold a special meeting at which all fellows of the College and other surgeons attending the Clinical Congress are invited to be present. The occasion of this special meeting of the society is the presentation of the Bigelow Medal to Dr. Allen O. Whipple, of New York, for his outstanding contributions to the advancement of surgery. The program follows:

Introduction: Irving J. Walker, M.D., President  
Address: "Present-day Surgery of the Pancreas," Allen O. Whipple, M.D.

Presentation of the Bigelow Medal: David Cheever, M.D.

### CLINICAL PATHOLOGICAL CONFERENCES

Selected fresh surgical specimens from the operative clinics of the various hospitals will be demonstrated each day with the aid of the Zeiss epidiascope in the Georgian Room of the Statler Hotel from 5:15 to 6:30 p.m. This is possible through the co-operation of the pathologists of the hospitals taking part in the Congress. The method of projection will enable all to see clearly the pathological processes involved.

By the use of fresh, rather than preserved material, chosen from each day's operative clinics, the surgeons interested in the various types of operation done during the day will be able to see the underlying pathology demonstrated and to hear a discussion of the clinical implications. Each conference will be conducted by a different pathologist from one of the co-operating hospitals or medical schools.

### PUBLICATION OF PROCEEDINGS

As in former years, the formal papers which are presented at the scientific sessions of the Congress will be presented in a special issue of the official journal of the College, "SURGERY, GYNECOLOGY, AND OBSTETRICS," published in February following the meeting. This issue is furnished without additional charge to all fellows, junior candidates, and others who register for the Congress as invited guests. The papers which are presented in connection with the Hospital Standardization Conference are published in subsequent issues of the *Bulletin of the American College of Surgeons*.

## ASSEMBLY OF INITIATES

The Assembly of Initiates will be held on Monday afternoon in John Hancock Hall. Dr. Evarts A. Graham, president, and Dr. Albert O. Singleton, Galveston, Texas, vice-president of the College, will preside. Dr. Bowman C. Crowell and Dr. Malcolm T. MacEachern will discuss "The Program of the American College of Surgeons." Initiates will then recite the fellowship pledge and greetings will be extended by Dr. W. Edward Gallie, Toronto, president-elect of the College. Closing remarks will be made by Dr. Irvin Abell, Chairman of the Board of Regents.

## NATIONAL AND REGIONAL FRACTURE COMMITTEES

The meeting of the National and Regional Fracture Committees, with Dr. Robert H. Kennedy, of New York, chairman of the National Committee, presiding, will be held on Thursday afternoon at the Copley-Plaza Hotel, when this assembly of surgeons will discuss the activities of the respective groups. Working in co-operation with the American Red Cross, other local organizations and public officials, these committees have exerted great influence in improving methods and facilities for the transportation of the injured. They have also made a concerted effort to improve the treatment of fractures in the hospitals of many communities. Pertinent problems will be discussed at the meeting of these committees.

## ANNUAL MEETING OF COMMITTEES

The annual meetings of the State and Provincial Judiciary, Credentials, and Executive Committees will be held on Wednesday morning in John Hancock Hall. These committees have an important function to perform in the College. The Credentials Committees and the Committees on Applicants constitute one of the largest and most carefully deliberate accrediting bodies which exist in the medical profession. Through this organization the standards of fellowship are maintained and each fellow of the College has a definite responsibility in this work. All members of these committees are urged to attend this important meeting.

## ANNUAL MEETING OF FELLOWS

The annual meetings of the governors and fellows will be held on Thursday afternoon in the ballroom of the Copley-Plaza Hotel. The American College of Surgeons has been a potent force which has not only raised the professional and ethical standards of surgery, but has also promoted good hospitalization and general improvement in the

practice of medicine in the United States and Canada. Each fellow of the College has a personal part in this work and may extend its influence materially in his local community. Hospital standardization alone offers him unlimited opportunity to provide better medical care for his patients in the hospital in which he works through continuous progress in applying the principles of the minimum standard. Other activities of the College have also received wide recognition by professional groups and the public as well, and together they present a vast educational program.

The annual meeting of the fellows affords officials of the College an opportunity to report on the work of the organization and to receive suggestions from those who have made possible the conduct of these activities. Every fellow of the College will want to attend this important meeting.

## MEDICAL MOTION PICTURES

Visual education plays an increasingly important rôle in the education of the surgeon. In recognition of this fact, an enlarged program of surgical motion pictures will be presented at headquarters which will include the latest available films on a variety of subjects. Schedules will be arranged so as not to conflict with the clinical program at hospitals or the scientific sessions, and will include both sound and silent, and color films, all of which have been approved by the Committee on Medical Motion Pictures of the College.

## HOSPITAL CONFERENCES

The Congress will open on Monday morning at 10:00 o'clock with the first session of the twenty-fourth annual Hospital Standardization Conference in the ballroom of the Copley-Plaza Hotel. The report of the 1941 hospital standardization survey—official announcement of the list of approved hospitals and hospitals approved for graduate training in surgery—will be made at this session. Dr. Evarts A. Graham, of St. Louis, president of the College, will preside. In addition there will be interesting discussions on the subjects of "Medical Preparedness," "The Preservation of Our Voluntary System of Hospitals," and "Maintaining the Control and Quality of the Professional Work in the Hospital." On Monday afternoon a panel discussion will deal with the timely subject of "Meeting the Problems of Rendering Adequate Care of the Patient and Maintaining Quality Standards of Service During the Present Period of Preparedness and National Emergency," with Dr. Nathaniel W. Faxon, of Boston, presiding.

Of special interest to surgeons, as well as hospi-

tal personnel, will be a series of panel discussions dealing with the efficient organization of the hospital. On Tuesday morning four panel discussions will deal with the essentials for efficiency of the hospital in (1) the Obstetrical Department, Dr. Harvey R. Matthews, Brooklyn, presiding; (2) the Orthopedic Department, Dr. Henry H. Kessler, Newark, New Jersey, presiding; (3) Organization and Functioning of the Medical Staff, Dr. Joseph C. Doane, Philadelphia, presiding; and (4) the Department of Anesthesia, Dr. Ralph T. Knight, Minneapolis, presiding. Two additional panel discussions will be held on Thursday morning; one on the "Essentials Pertaining to an Efficient Department of Urology" will be led by Dr. George F. Cahill, New York, and the other, "Essentials Pertaining to an Efficient Department of Ophthalmology and Otolaryngology," by Drs. Conrad Behrens and Marvin Jones, of New York.

In preparing this portion of the program, organizations representing the specialty groups have been invited to participate. Special consideration will be given in this series of meetings to the important subject of graduate training in surgery. It is hoped that through this means the fellows of the College may become better acquainted with its program of hospital activities, which is aimed at improvement of the environment in which the surgeon is working—the hospital.

On Thursday afternoon, Dr. Robin C. Buerki, of Philadelphia, will lead a round-table conference on "Pertinent Problems Emanating from a Complete Survey of the Hospital Field." An ample opportunity will be given those present to submit questions which are not on the special program.

The entire program as detailed in the following pages will hold great interest for members of medical staffs, trustees, administrators, and other hospital personnel. On Tuesday afternoon several pertinent subjects will be presented including "The Organization of a Blood Transfusion Department in a General Hospital," by Drs. Leo M. Zimmerman and Sidney O. Levinson, Chicago. Following these papers a sound motion picture on the subject of "The Proper Use and Care of Hypodermic Needles" will be shown. Tuesday evening's session will be of particular interest to hospital trustees when the subject of the panel discussion will be "The Hospital Trustee in His Relationships and Responsibilities," led by Raymond P. Sloan, of New York.

On Wednesday morning, a joint session with the American Association of Medical Record Librarians will be held, with Dr. Robin C. Buerki, of Philadelphia, presiding. Wednesday evening

will be given over to the showing of medical motion pictures for hospital personnel, including a new film, "White Battalions—Serving All Mankind."

For Wednesday afternoon a series of demonstrations in the local hospitals has been arranged. Those who are acquainted with Boston are fully aware of the inspiration furnished by the privilege of inspecting one of the country's greatest hospital centers. Those who have not had that privilege have a memorable experience in store.

At both the Clinical Congress and the sectional meetings of the College during recent years, the breakfast hospital conferences have been especially well attended. In Boston, such a conference will be held on Tuesday morning when there will be a "Forum on Fundamental Problems of Hospital Administration," sponsored by the American College of Hospital Administrators, in co-operation with the American College of Surgeons.

On Wednesday morning, the breakfast conference will be sponsored by the Boston Medical Record Librarians Association, in co-operation with the College, when there will be held a "Forum on Fundamental Considerations in the Art and Science of Medical Record Keeping." The Thursday morning breakfast conference will be devoted to hospital public relations. The plan is to allow each speaker ten minutes to present his subject, following which everyone will be called upon to give his reaction to the problem under discussion. Attendance at these meetings will necessarily be limited and arrangements will be made for advance registration.

One of the most important features of the hospital conference will be the daily consultation service from 4:30 to 6:00 p. m. This service affords an opportunity for everyone attending the meeting to consult with recognized leaders in the hospital field on any question or problem on which specific information is desired.

#### ADVANCE REGISTRATION

The hospitals and medical schools of the Boston area afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, attendance at the Congress will be limited to the number that can be comfortably accommodated at the clinics. The limit of attendance will be based on a survey determining the available facilities in the participating hospitals and schools. It is expected, therefore, that surgeons who wish to attend the Congress will register in advance. A registration fee will be required in order to provide funds with which to meet expenses of the meeting. A formal receipt

will be issued to each surgeon registering in advance which will be exchanged for a general admission card upon presentation at headquarters during the Congress. This card, which is not transferable, must accompany all requests for clinic tickets and be presented for admission to the scientific sessions.

A resolution adopted by the Board of Regents provides that the registration fee for fellows of the College and endorsed junior candidates shall be \$5.00; that no fee for the 1941 Clinical Congress shall be required of initiates (class of 1941); that the fee for surgeons who are not fellows, attending as invited guests of the College, shall be \$10.00.

As in previous years, admission to clinics and demonstrations in the hospitals and certain of the scientific meetings at headquarters will be controlled by means of tickets. This plan provides for the distribution of visiting surgeons at the various clinics and other meetings, and helps to insure against overcrowding. The number of clinic tickets issued will be limited in each case to the capacity of the room in which the clinic is held. It should be pointed out that the clinical program as published in the following pages and also in the official program to be distributed at the Congress, obviously cannot include all of the detailed information regarding operative clinics and demonstrations scheduled for the various hospitals. The complete and final program will be provided from day to day, posted in the form of bulletins at headquarters each afternoon for the succeeding day, and published in the *Daily Clinical Bulletin* for distribution each morning. Visiting surgeons are urged to consult the bulletins posted at headquarters and the *Daily Clinical Bulletin* in selecting the clinics they wish to attend, and in making requisitions for clinic tickets. Co-operation in making the clinic ticket plan a success will be greatly appreciated.

#### HEADQUARTERS AND TECHNICAL EXHIBITION

Headquarters for the Congress will be established at the Statler and Copley-Plaza Hotels where there are ample facilities for accommodating the Congress. All of the public rooms have been reserved for the exclusive use of the College during the five-day meeting. Registration for visiting surgeons and their ladies, the Technical Exhibition, executive offices of the College, and certain scientific sessions and medical motion picture exhibitions will be located in the Statler Hotel. Registration for those attending the hospital conference, exhibits of College activities, and the morning, afternoon, and evening hospital conferences will be located in the Copley-Plaza Hotel.

The evening scientific sessions on Tuesday, Wednesday, and Thursday will also be held at the Copley-Plaza.

The Technical Exhibition, registration desk for attending surgeons, clinic ticket and information bureau will be located in the ballroom on the mezzanine floor of the Statler Hotel. Additional space for the exhibition will be provided in the Assembly Room and the mezzanine lounge adjacent to the ballroom. Leading manufacturers of surgical instruments and supplies, sutures, dressings, pharmaceuticals, operating room equipment of all kinds, and publishers of medical books will be represented in the exhibition. It will provide an opportunity for surgeons and hospital visitors to carefully inspect the finest modern products of all those industries which are helping to improve the service of hospitals and surgeons.

#### REGISTRATION FOR VISITING LADIES

A registration desk and information bureau for the visiting ladies will be established on the mezzanine floor of the Statler Hotel, under the sponsorship of the ladies of the Women's Auxiliary. An invitation is extended to wives, daughters, and friends of fellows attending the Clinical Congress to register and avail themselves of the information bureau which will be open daily during the Congress, offering assistance in locating visiting friends, shopping, sight-seeing and other matters.

#### SPECIAL TRAIN TO BOSTON VIA NEW YORK CENTRAL LINES

For the convenience of surgeons living in the central, western, southwestern and northwestern states, who will attend the Clinical Congress in Boston, arrangements are being made by the New York Central Lines to provide a special train leaving Chicago at 1 p.m. on Sunday, November 2, arriving in Boston at 9 a.m. on Monday. This special train will be equipped with cars of latest design, including club, lounge, observation, room cars of all types and standard Pullman cars. No extra fare will be charged. Fellows are urged to make their reservations for this special train at the earliest possible date, making application to the office of the Assistant General Passenger Agent, New York Central Lines, LaSalle Street Station, Chicago.

#### RAILROAD FARES

As no special rates have been authorized by the railroads of the United States or Canada for the 1941 Clinical Congress in Boston, in accordance with the policy adopted by the railroads, no certificates will be required. However, round-trip

tal personnel, will be a series of panel discussions dealing with the efficient organization of the hospital. On Tuesday morning four panel discussions will deal with the essentials for efficiency of the hospital in (1) the Obstetrical Department, Dr. Harvey R. Matthews, Brooklyn, presiding; (2) the Orthopedic Department, Dr. Henry H. Kessler, Newark, New Jersey, presiding; (3) Organization and Functioning of the Medical Staff, Dr. Joseph C. Doane, Philadelphia, presiding; and (4) the Department of Anesthesia, Dr. Ralph T. Knight, Minneapolis, presiding. Two additional panel discussions will be held on Thursday morning; one on the "Essentials Pertaining to an Efficient Department of Urology" will be led by Dr. George F. Cahill, New York, and the other, "Essentials Pertaining to an Efficient Department of Ophthalmology and Otolaryngology," by Drs. Conrad Behrens and Marvin Jones, of New York.

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## PROGRAMS FOR EVENING SESSIONS

*Presidential Meeting and Convocation—Monday, 8:00 p.m.—Symphony Hall*

EVARTS A. GRAHAM, M.D., St. Louis; President, American College of Surgeons, Presiding.

Processional—Officers, Regents, and Honorary Guests.

Invocation.

Address of Welcome. LELAND S. MCKITTRICK, M.D., Boston; Chairman, Committee on Arrangements.

Introduction of Foreign Guests. ARTHUR W. ALLEN, M.D., Boston; Vice Chairman, Board of Regents.

Address of Retiring President: American Surgery in a Changing World. EVARTS A. GRAHAM, M.D., St. Louis.

Inauguration of Officers:

President: W. EDWARD GALLIE, M.D., Toronto.

First Vice President: CLARENCE G. TOLAND, M.D., Los Angeles.

Second Vice President: ALBERT C. FURSTENBERG, M.D., Ann Arbor.

Presentation of Initiates for Fellowship. IRVIN ABELL, M.D., Louisville; Chairman, Board of Regents.

Conferring of Fellowships by the President. W. EDWARD GALLIE, M.D., Toronto.

Conferring of Honorary Fellowships. The President.

Medical Records Prize Award.

*Tuesday, 8:00 p.m.—Ballroom, Copley-Plaza Hotel*

CLARENCE G. TOLAND, M.D., Los Angeles, Vice-President, American College of Surgeons, Presiding.

Annual Oration on Surgery: Some Lessons Learned in the Great War. W. EDWARD GALLIE, M.D., Toronto.

Use of Female Sex Hormones in Clinical Practice. EDWIN C. HAMBLIN, M.D., Durham, N. C.

The Prevention and Treatment of Tetanus. WARFIELD M. FIROR, M.D., Baltimore.

The Care of the Slightly Wounded. WILLIAM DARRACH, M.D., New York.

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W. EDWARD GALLIE, M.D., Toronto, President, American College of Surgeons, Presiding.

On the Surgical Problems of Modern Warfare. REAR ADMIRAL GORDON GORDON-TAYLOR, Surgeon, Royal Navy, O.B.E., F.R.C.S. (Eng.), London, England.

Endocrine Aspects of Chronic Cystic Mastitis. HOWARD C. TAYLOR, JR., M.D., New York.

Penetrating Wounds of the Heart and Pericardium. R. ARNOLD GRISWOLD, M.D., and C. H. MAGUIRE, M.D., Louisville.

Oration on Fractures and Other Traumas: The General Surgeon's Approach to Problems Presented by Fractures and Other Traumas. WALTER ESTELL LEE, M.D., Philadelphia.

*Thursday, 8:00 p.m.—Ballroom, Copley-Plaza Hotel*

ARTHUR W. ALLEN, M.D., Boston, Vice-Chairman, Board of Regents, American College of Surgeons, Presiding.

Functional Disturbances of the Hepatic and Choledochous Ducts. PROFESSOR PABLO LUIS MIRIZZI, M.D., Cordoba, Argentina.

Carcinoma of the Stomach (Diagnostic Methods and Therapy). HOWARD K. GRAY, M.D., Rochester, Minn.

Non-penetrating Wounds of the Abdomen. W. L. ESTES, JR., M.D., Bethlehem, Pa.

Adrenal Cortical Tumors; the Types of Non-hormonal and Hormonal Tumors. GEORGE F. CAHILL, M.D., New York.

Evaluation of Blood and Blood Substitutes. ALFRED BLALOCK, M.D., Nashville.

tickets to Boston, sold at less than double the regular one-way fare, will be available from points in the United States and Canada. Return limit privileges of such round-trip tickets are liberal but are not uniform in all sections of the country. In most instances the return limit is 30 days or more. Surgeons planning to attend the Congress should consult local ticket agents several days in advance of the date of the meeting for complete information as to fares, routes, stopover privileges, etc.

#### BOSTON HOTELS AND THEIR RATES

In addition to the headquarters hotels, the Statler and Copley-Plaza, there are a number of first-class hotels within a short distance of headquarters. These will provide ample facilities at reasonable rates. It is suggested that reservations for hotel accommodations be made well in advance of the meeting. The following hotels are recommended by the committee:

	Minimum Rate with Bath	
	Single	Double
Bellevue, 21 Beacon Street	\$3 00	\$4 50
Bradford, 275 Tremont Street	3 00	4 50
Brunswick, 520 Boylston Street	3 00	4 00
Buckminster, 645 Beacon Street	2 50	4 00
Copley-Plaza, 138 St. James Avenue	4 00	6 00
Copley Square, 47 Huntington Avenue	2 75	4 00
Kenmore, 490 Commonwealth Avenue	3 50	5 00
Lenox, Lxeter Street	3 00	3 50
Lincolnshire, 20 Charles Street	3 00	5 00
Parker House, 60 School Street	3 50	5 00
Ritz-Carlton, 15 Arlington Street	5 00	8 00
Sheraton, 91 Bay State Road	3 00	5 00
Somerset, 400 Commonwealth Avenue	3 50	6 00
Statler, Park Square	3 50	5 00
Touraine, 62 Boylston Street	3 50	5 00
Vendome, 160 Commonwealth Avenue	3 00	4 00
Westminster, 124 St. James Avenue	2 50	4 00

#### COMMITTEE ON ARRANGEMENTS

Leland S. McKittrick	Frank H. Lahey
Chairman	Charles C. Lund
Richard H. Sweet	Donald Munro
Secretary	Charles G. Muxter
Arthur W. Allen	Frank R. Ober
Edward D. Churchill	Robert B. Osgood
Howard M. Clute	Frank A. Pemberton
E. Granville Crabtree	George L. Tobey, Jr.
Elhott C. Cutler	Frederick H. Verhoeff
Frederick C. Irving	Irving J. Walker
William E. Ladd	Shields Warren

#### HOSPITALS AND REPRESENTATIVES

Beth Israel Hospital—Jacob Fine	
Beverly Hospital—Richard E. Alt	
Evangeline Booth Maternity Hospital—W. J. McDonald	
Boston City Hospital—Otto J. Hermann	
Boston Lyngin Hospital—Frederick C. Irving	
Peter Bent Brigham Hospital—Elliott C. Cutler	
Robert Breck Brigham Hospital—John G. Kuhns	
Carney Hospital—A. M. Fraser	
Children's Hospital—Thomas H. Lanman	
Corey Hill Hospital—Richard H. Overholt	
Faulkner Hospital—E. L. Young	
Free Hospital for Women—Frank A. Pemberton	
Collis P. Huntington Memorial Hospital—C. C. Summons	
Lakeville State Sanatorium—George W. VanGorder	
Malden Hospital—E. J. Reynolds	
Massachusetts Eye and Ear Infirmary—F. H. Verhoeff	
Massachusetts General Hospital—Arthur W. Allen	
Massachusetts Memorial Hospital—Frank E. Barton	
New England Baptist Hospital—N. W. Swinton	
New England Deaconess Hospital—B. P. Colcock	
New England Hospital for Women and Children—L. D. Adams	
New England Medical Center—Samuel H. Proger	
Newton Hospital—E. D. Leonard	
Palmer Memorial Hospital—Leland S. McKittrick	
Pondville Hospital—E. M. Daland	
St. Elizabeth's Hospital—Joseph Stanton	
Salem Hospital—Walter G. Phippen	
United States Marine Hospital—R. L. Waugh	
United States Naval Hospital—J. J. A. McMullan	

## PROGRAMS FOR EVENING SESSIONS

*Presidential Meeting and Convocation—Monday, 8:00 p.m.—Symphony Hall*

EVARTS A. GRAHAM, M.D., St. Louis; President, American College of Surgeons, Presiding.

Processional—Officers, Regents, and Honorary Guests.

Invocation.

Address of Welcome. LELAND S. MCKITTRICK, M.D., Boston; Chairman, Committee on Arrangements.

Introduction of Foreign Guests. ARTHUR W. ALLEN, M.D., Boston; Vice Chairman, Board of Regents.

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Evaluation of Blood and Blood Substitutes. ALFRED BLALOCK, M.D., Nashville.



## SURGERY, GYNECOLOGY AND OBSTETRICS

### PROGRAMS FOR EVENING SESSIONS

#### OPHTHALMOLOGY

*Tuesday, 8:00 p.m. — Room B, Statler Hotel*

EDWIN B. DUNPHY, M.D., Boston, Presiding

Symposium: Surgery of Heterophoria and Heterotropia.

Preoperative Diagnosis and Treatment. JAMES W. WHITE, M.D., New York.

Trends in the Surgery of Heterotropia. PROFESSOR MOACYR EYCK ALVARO, M.D., Sao Paulo, Brazil.

Surgical Management of Heterophoria. DERRICK T. VAIL, JR., M.D., Cincinnati.

Results of Operation and Causes of Failure. WILLIAM THORNWALL DAVIS, M.D., Washington.

*Thursday, 8:00 p.m. — Room B, Statler Hotel*

LAWRENCE T. POST, M.D., St. Louis, Member, Advisory Council for Ophthalmology, American College of Surgeons, Presiding.

Symposium: Principles of Ophthalmic Surgery.

Surgical Anatomy of the Eye. F. BRUCE FRALICK, M.D., Ann Arbor, Mich.

Refinements of General Surgical Technique as Applied to Ophthalmology. CONRAD BERENS, M.D., New York.

Management of Surgical Complications. THOMAS D. ALLEN, M.D., Chicago.

#### OPHTHALMOLOGY AND OTORHINOLARYNGOLOGY

*Wednesday, 8:00 p.m. — Room A, Statler Hotel*

HARRY S. GRADLE, M.D., Chicago, Regent, American College of Surgeons, Presiding

Symposium: Neurological Surgery as Related to the Eye and Ear

Intracranial Infections and Their Spread from the Ear and from the Sinuses. ALBERT C. FURSTENBERG, M.D., Ann Arbor, Mich.

Retrobulbar Neuritis in Relation to Sinus Disease. JAMES B. COSTEN, M.D., St. Louis.

Tumors of the Acoustic Nerve. BYRON STOOKEY, M.D., New York.

Major Surgery of the Orbit. HOWARD C. NAFFZIGER, M.D., San Francisco.

Interpretation of Perimetric Fields of Vision as Manifested in Intracranial Disease. ALBERT D. RUEDEMANN, M.D., CLEVELAND.

#### OTORHINOLARYNGOLOGY

*Tuesday, 8:00 p.m. — Room A, Statler Hotel*

ALBERT C. FURSTENBERG, M.D., Ann Arbor, Mich., Vice-President, American College of Surgeons, Presiding.

Sulfonamide Drugs in the Treatment of Suppurative Otitis Media and Mastoiditis. JAMES H. MAXWELL, M.D., Ann Arbor, Mich.

Refinements in the Technique of Laryngectomy. WAITMAN F. ZINN, M.D., Baltimore.

The Otology of Cranio-cerebral Injuries. WILLIAM E. GROVE, M.D., Milwaukee, Wis.

*Thursday, 8:00 p.m. — Room A, Statler Hotel*

HARRIS P. MOSHER, M.D., Boston, Presiding

Symposium. The Salivary Gland

Benign and Locally Malignant Tumors. ALBERT O. SINGLETON, M.D., Galveston, Texas.

Malignant Tumors. LEROY A. SCHALL, M.D., Boston.

Infections. AUGUST L. BECK, M.D., New Rochelle, N. Y.

## PROGRAMS FOR AFTERNOON SESSIONS

## CANCER SYMPOSIUM

*Tuesday, 2 p.m.—Ballroom, Copley-Plaza Hotel*

FRANK E. ADAIR, M.D., New York, Chairman, Cancer Committee, presiding.  
 Radical Surgical Treatment for Carcinoma of the Cardiac End of the Stomach. JOHN H. GARLOCK, M.D., New York.

Precancerous Lesions. CORNELIUS P. RHOADS, M.D., New York.

Trends in Cancer Research. CARL VOEGTLIN, Ph.D., Bethesda, Md.

Standard Classified Nomenclature of Diseases and Operations, with Especial Reference to Tumors. EDWIN P. JORDAN, M.D., Chicago.

The Role of the Radiologist in the Cancer Clinic. GEORGE W. HOLMES, M.D., Boston.

## SYMPOSIUM ON FRACTURES AND OTHER TRAUMAS

*Wednesday, 2:00 p.m.—Ballroom, Copley-Plaza Hotel*

ROBERT H. KENNEDY, M.D., New York; Chairman, Committee on Fractures and Other Traumas, Presiding.  
 Gunshot Wounds of the Abdomen. AMBROSE H. STORCK, M.D., New Orleans.

A Critical Survey of Ten Years' Experience with Fractures of the Neck of the Femur. MATHER CLEVELAND, M.D., New York.

Factors in the Choice of Material for Bone Plates and Screws. CHARLES S. VENABLE, M.D., San Antonio, Texas.

Treatment of Burns. GROVER C. PENBERTHY, M.D., Detroit.

Results in Cases of Compound Fractures Followed by Osteomyelitis. STANTON K. LIVINGSTON, M.D., Veterans Administration Facility, White River Junction, Vermont.

## ASSEMBLY OF INITIATES

*Monday, 3:00 p.m.—John Hancock Hall, 90 St. James Avenue*

EVARTS A. GRAHAM, M.D., St. Louis, President, Presiding.

Processional—Officers, Regents, and Governors.

Opening Remarks. EVARTS A. GRAHAM, M.D., St. Louis, President.

The Program of the American College of Surgeons. ALBERT O. SINGLETON, M.D., Galveston, Vice President.

The Department of Clinical Research: Cancer; Fractures and Other Traumas; Bone Sarcoma; Hall of the Art and Science of Surgery. BOWMAN C. CROWELL, M.D., Chicago, Associate Director.

Hospital Standardization; Sectional Meetings; Graduate Training in Surgery; Library and Department of Literary Research. MALCOLM T. MACEachern, M.D., Chicago, Associate Director.

The Fellowship Pledge. Recital by Initiates.

Greetings to the Initiates. W. EDWARD GALLIE, M.D., Toronto, President-elect.

Fellowship in the College. IRVIN ABELL, M.D., Louisville, Chairman, Board of Regents.

Signing of the Fellowship Roll. The Initiates.

Reception by the Officers and Regents for the Fellows and Initiates and members of their families.

*Wednesday, 3:30 to 5:00 p.m.—Staller Hotel*

*Room B, Mezzanine Floor*

Graduate Training in Surgery in Hospitals (Second Session) ROBIN C. BUECKI, M.D., Philadelphia, Presiding.

Collaborators: DAVID H. BALLON, M.D., Montreal; GEORGE F. CAHILL, M.D., New York, EDWARD D. CHURCHILL, M.D., Boston, JOHN R. FRASER, M.D., Montreal, W. EDWARD GALLIE, M.D., Toronto; HARRY S. GRADLE, M.D., Chicago, DALLAS B. PHEMISTER, M.D., Chicago, STANLEY J. SEEGER, M.D., Milwaukee, Wis.; PHILIP D. WILSON, M.D., New York.

*Georgian Room, Mezzanine Floor*

Postoperative Pulmonary Complications. LEO ELOFSSER, M.D., San Francisco, Presiding

Collaborators: HENRY K. BEECHER, M.D., Boston, STUART W. HARRINGTON, M.D., Rochester, Minn.; RICHMOND L. MOORE, M.D., New York.

*Room A, Mezzanine Floor*

Disruption of Abdominal Wounds. FRANK GLENN, M.D., New York, Presiding

Collaborators: LAWRENCE S. FALLIS, M.D., Detroit; L. KRAEER FERGUSON, M.D., Philadelphia; HILGER P. JENKINS, M.D., Chicago.

*Room C, Mezzanine Floor*

Continuous Spinal Anesthesia. WILLIAM T. LEMMON, M.D., Philadelphia, Presiding

Collaborators: H. H. BRADSHAW, M.D., Winston-Salem, N. C.; RALPH T. KNIGHT, M.D., Minneapolis; EDWARD B. TUOHY, M.D., Rochester, Minn.

*Thursday, 3:30 to 5:00 p.m.—Staller Hotel*

*Room C, Mezzanine Floor*

Treatment of Chronic Cervicitis. GEORGE H. GARDNER, M.D., Chicago, Presiding

Collaborators: JOHN C. BURCH, M.D., Nashville, J. MASON HUNDLEY, JR., M.D., Baltimore, JOE V. MEIGS, M.D., Boston

*Room A, Mezzanine Floor*

Chemotherapy in Wound Healing. EDWARD L. HOWES, M.D., New York, Presiding

Collaborators: HILGER P. JENKINS, M.D., Chicago, FRANK L. MELENFY, M.D., New York, J. ROSS VEAL, M.D., Washington.

*Georgian Room, Mezzanine Floor*

The Treatment of the Wound in Compound Fractures. CLAY RAY MURRAY, M.D., New York, Presiding

Collaborators: R. ARNOLD GRISWOLD, M.D., Louisville, J. ALBERT KRY, M.D., St. Louis, HENRY C. MARBLE, M.D., Boston

*Room B, Mezzanine Floor*

Anesthesia for Surgical Procedures within the Upper Abdomen. RALPH M. FOVELL, M.D., Hartford, Conn., Presiding

Collaborators: HENRY K. BEECHER, M.D., Boston, HOWARD K. GRAY, M.D., Rochester, Minn.; HENRY S. RUTH, M.D., Merion, Pa.

*Salle Moderne*

Contributions to Medical Progress through Postmortem Examinations. ALAN R. MORITZ, M.D., Boston, Presiding

Collaborators: A. O. GETTLER, Ph.D., New York, HARRISON S. MARTLAND, M.D., Newark, N. J.

*Friday, 1:30 to 3:00 p.m.—Staller Hotel*

*Room B, Mezzanine Floor*

Chemotherapy in Genitourinary Infections or in Infections of the Prostatic Gland. EDWIN P. ALYEA, M.D., Durham, N. C., Presiding

Collaborators: GEORGE F. CAHILL, M.D., New York, GEORGE C. PRATHER, M.D., Boston

*Room C, Mezzanine Floor*

Diseases of the Esophagus. ALTON OCHSNER, M.D., New Orleans, Presiding.

Collaborators: CARL EGGERS, M.D., New York; FRANK H. LAHEY, M.D., Boston; GABRIEL TUCKER, M.D., Philadelphia.

*Georgian Room, Mezzanine Floor*

The Management of the Perforated Appendix, Early and Late. HENRY K. RANSOM, M.D., Ann Arbor, Mich., Presiding.

Collaborators: J. MONTGOMERY DEEVER, M.D., Philadelphia, CLARENCE E. GARDNER, JR., M.D., Durham, N. C.; E. ERIC LARSON, M.D., Los Angeles.

*Room A, Mezzanine Floor*

Experience with the Miller-Abbott Tube. ALLEN O. WHIPPLE, M.D., New York, Presiding.

Collaborators: WILLIAM O. ABBOTT, M.D., Philadelphia; CHARLES G. JOHNSTON, M.D., Detroit; ANGUS MCLACHLIN, M.D., Toronto.

*Friday, 3:30 to 5:00 p.m.—Statler Hotel*

*Room B, Mezzanine Floor*

Fractures of the Facial Bones. LLOYD NOLAN, M.D., Fairfield, Ala., Presiding.

Collaborators: ROBERT H. IVY, M.D., Philadelphia; CARL W. WALDRON, M.D., Minneapolis; CHARLES H. WILSON, M.D., New Orleans.

*Georgian Room, Mezzanine Floor*

Surgical Diseases of the Colon. CHARLES W. MAYO, M.D., Rochester, Minn., Presiding.

Collaborators: THOMAS G. ORR, M.D., Kansas City, Mo.; HOWARD PATTERSON, M.D., New York; J. WILLIAM THOMPSON, M.D., St. Louis.

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## GROUP CLINICAL CONFERENCES

### OPHTHALMOLOGY AND OTORHINOLARYNGOLOGY

*Tuesday, 11:00 a.m.—Statler Hotel*

Surgery of Squint. JOHN H. DUNNINGTON, M.D., New York, Presiding.

Treatment of Sinus Disease in Children. SAMUEL SALINGER, M.D., Chicago, Presiding.

*Wednesday, 11:00 a.m.—Statler Hotel*

Surgery of the Tear Passages. WALTER S. ATKINSON, M.D., Watertown, N. Y., Presiding.

Indications for Surgery of the Nose and Throat in Diabetics. WESTLEY M. HUNT, M.D., New York, Presiding.

*Thursday, 11:00 a.m.—Statler Hotel*

Surgery of the Orbit. ALGERNON B. REESE, M.D., New York, Presiding.

Surgical Treatment of Deafness. SAMUEL J. KOPETZKY, M.D., New York, Presiding.

## ANNUAL MEETING, BOARD OF GOVERNORS

*Wednesday, 12:00 m.—Salon, Copley-Plaza Hotel*

W. EDWARD GALLIE, M D., Toronto; President, American College of Surgeons, Presiding.

Statement by the Chairman of the Board of Regents. IRVIN ABELL, M D., Louisville.

Types of Problems Encountered by the Administrative Board and the Central Committee on Credentials and Methods of Dealing with Them: FREDERIC A. BESLEY, M D., Waukegan, Secretary; MALCOLM T. MACEachern, M D., Chicago, Chairman, Administrative Board, BOWMAN C. CROWELL, M D., Chicago, Vice Chairman, Administrative Board.

Discussion by the Governors and Regents.

## ADJOURNED MEETING, BOARD OF GOVERNORS

*Thursday, 1:30 p.m.—Ballroom, Copley-Plaza Hotel*

Report of Committee on Nominations to the Board of Governors.

## ANNUAL MEETING, FELLOWS OF THE COLLEGE

*Thursday, 1:45 p.m.—Ballroom, Copley-Plaza Hotel*

W. EDWARD GALLIE, M D., Toronto, President, American College of Surgeons, Presiding

Report of Committee on Nominations to the Fellows.

Library and Department of Literary Research MISS L. MARGUERITE PRIME, Chicago, Librarian

Financial Report DALLAS B. PHENISTER, M.D., Chicago, Treasurer

Departmental Reports: (a) Hospital Standardization (b) Work of Credentials Committees, Committees on Applicants, and Committee on History Reviews (c) State and Provincial Sectional Meetings (d) Medical Motion Pictures. (e) Public Relations. MALCOLM T. MACEachern, M.D., Chicago; Associate Director.

Graduate Training in Surgery—General Surgery and the Surgical Specialties DALLAS B. PHENISTER, M.D., Chicago; Chairman, Committee on Graduate Training in Surgery

Hall of the Art and Science of Surgery. GEORGE CRILE, M D., Cleveland; Chairman, Committee on the Hall of the Art and Science of Surgery.

Committee on Cancer FRANK E. ADAIR, M D., New York, Chairman

Committee on Fractures and Other Traumas. ROBERT H. KENNEDY, M D., New York, Chairman

Department of Clinical Research BOWMAN C. CROWELL, M D., Chicago, Associate Director.

College Administration FREDERIC A. BESLEY, M D., Waukegan, Secretary.

Fellowship Obligations and Opportunities. ARTHUR W. ALLEN, M D., Boston; Vice Chairman, Board of Regents

The College in Its Relation to National Defense. IRVIN ABELL, M D., Louisville, Chairman, Board of Regents.

## COMMITTEE MEETINGS

IRVIN ABELL, M.D., Louisville; Chairman, Board of Regents, Presiding.

## STATE AND PROVINCIAL JUDICIARY COMMITTEES

*Wednesday, 9:30 a.m.—John Hancock Hall, 90 St. James Avenue*

Statement by the Chairman of the Board of Regents.

Selection and appointment of judiciary committees.

Procedure in dealing with judiciary cases.

Types of cases referred to the judiciary committees.

Discussion by Fellows and Regents of the College.

## STATE AND PROVINCIAL EXECUTIVE COMMITTEES

*Wednesday, 10:00 a.m.—John Hancock Hall, 90 St. James Avenue*

Statement by the Chairman of the Board of Regents.

Sectional Meetings Held in 1941 and Plans for Sectional Meetings in 1942.

Comments on Sectional Meetings in 1941, by the Chairmen of the Committees on Local Arrangements:

1. Minneapolis, Minnesota. WILLIAM A. HANSON, M.D.

2. Pittsburgh, Pennsylvania. HOLLAND H. DONALDSON, M.D.

3. Salt Lake City, Utah. RALPH T. RICHARDS, M.D.

Discussion by the Fellows and Regents of the College.

## CREDENTIALS COMMITTEES AND COMMITTEES ON APPLICANTS

*Wednesday, 10:30 a.m.—John Hancock Hall, 90 St. James Avenue*

Statement by the Chairman of the Board of Regents.

Summary of Work of Credentials Committees and Committees on Applicants, 1941.

Demonstration—Interviewing a Candidate for Fellowship by a Committee on Applicants. CHARLES S. KENNEDY, M.D., Detroit, Chairman; ELMER R. ARN, M.D., Dayton; FRANK K. BOLAND, M.D., Atlanta; VERNE C. HUNT, M.D., Los Angeles; FREDERIC V. HUSSEY, M.D., Providence; CHARLES B. PUESTOW, M.D., Chicago; GEORGE K. RHODES, M.D., San Francisco.

The Junior Candidate. JAMES E. THOMPSON, M.D., New York.

Discussion by the Fellows and Regents of the College.

## FORUM ON FUNDAMENTAL SURGICAL PROBLEMS

*Tuesday, Wednesday, Thursday, Friday, 9:30 a. m.—Ballroom, Copley-Plaza Hotel*

OWEN H. WANGENSTEEN, M.D., Minneapolis, Chairman of Committee, Presiding.

Presentation of the results of clinical and experimental research on problems related to general surgery and the surgical specialties being currently conducted by the departments of surgery in many of our medical schools. Detailed programs for these sessions will be published in the official program and the *Daily Clinical Bulletin*.

# SURGERY, GYNECOLOGY AND OBSTETRICS

## ANNUAL HOSPITAL STANDARDIZATION CONFERENCE

578

**Monday, 10:00 a.m. — Ballroom, Copley-Plaza Hotel**  
**EVARTS, A. GRAHAM, M.D., St. Louis, President, American College of Surgeons, presiding**  
**Address of the President — The Hospital Program of the American College of Surgeons**  
**Report of the 1941 Hospital Standardization Survey — Official Announcement of the List of Approved Hospitals. IRVING ABELL, M.D., Louisville; Chairman, Board of Regents, and EARLE W. WILLIAMSON, M.D., Chicago, Assistant Director, American College of Surgeons**  
**Report on Graduate Training in Surgery. DALLAS B. FLEMING, M.D., Chicago; Chairman, Committee on Graduate Training in Surgery, and HAROLD FARNHEART, M.D., Chicago, Assistant Director, American College of Surgeons**  
**Important Legislative, Preparedness and Emergency Problems Now Facing Hospitals. BERT W. CALDWELL, M.D., Chicago, Executive Secretary, American Hospital Association.**  
**The Preservation of Our Voluntary System of Hospitals. REV. ALPHONSE M. SCHWITALLA, S.J., St. Louis, President, Catholic Hospital Association**  
**The Responsibility of the Medical Staff in Maintaining Control and Quality of the Professional Work in the Hospital. MERRILL N. FOOTE, M.D., Brooklyn**  
**National Events and Their Effect on Personnel Relations. FRANK J. WALTER, Denver**  
**Hospital Preparedness in the Defense Program. JAMES A. HAMILTON, New Haven, Conn.**

**Monday, 2:00 p.m. — Ballroom, Copley-Plaza Hotel**  
**Panel Round Table Conference. Meeting the Problems of Rendering Adequate Care of the Patient and Maintaining Quality Standards of Service During the Present Period of Preparedness and National Emergency. NATHANIEL W. FAXON, M.D., Boston, presiding**  
**Discussion from the standpoint of professional personnel. Medical Staff. NORBERT A. WILHELM, M.D., Boston**  
**Resident Medical Staff. CLAUDE W. MCNER, M.D., New York**  
**Nursing Staff. SALLY JOHNSON, R.N., Boston**  
**Discussion from the standpoint of medical surgical and hospital equipment, instruments and supplies. Scientific Equipment and Instruments. D. H. PALMER, New York**  
**Surgical Dressings, Rubber Goods and Other Supplies. L. M. ARROWSMITH, Brooklyn**  
**Surgical Ligatures, Pharmaceuticals and Chemicals. IVERETT W. JONES, Albany, N.Y.**  
**Discussion from the standpoint of operating costs. Foodstuffs, Supplies of All Kinds, Commodities, etc. MIRIAM C. RYAN, R.N., Syracuse, N.Y.**  
**Salaries and Wages. ABRAHAM ONOFF, Pittsburgh**  
**Supplementary Revenue. Subsidies, Gifts, Donations, Endowments, etc. OLIVER H. BARTINE, Bridgeport, Conn.**  
**General Discussion. Other related subjects may also be presented if time permits**

**Monday, 3:30 p.m. — Foyer, Copley-Plaza Hotel**  
**Consultation Service. Opportunity will be afforded every one attending the Hospital Standardization Conference to consult with recognized leaders in the hospital field on any question or problem on which specific in-**

formation is desired. A consultation service will be available at the time and place specified in the program, by means of pre-arranged information stations, on six different phases of hospital service data. This service will be provided by leaders in the various fields of hospital administration and management. Administrative Practices and Policies. EDGAR C. HAYMON, Paterson, N.J.

Anesthesia Service. E. B. TROHY, M.D., Rochester, Minn.  
 Clinical Laboratory and Pathological Service. WILMAR M. ALLEN, M.D., Hartford, Conn.  
 Control of Major Surgery in the Hospital. F. MAC DONALD STANTON, M.D., Schenectady, N.Y.  
 Food Service in the Hospital — Diet Therapy. GENEVA MARBLE, Boston  
 Plans for Hospitals in the Present Emergency. OLIVER G. PRATT, Salem, Mass.

**Tuesday, 7:45 a.m. — Salon, Copley-Plaza Hotel**  
**Breakfast Conference, Sponsored by the American College of Hospital Administrators in co-operation with the American College of Surgeons. Forum on Fundamental Problems of Hospital Administration. SCOTT WHITCHEL, New Bedford, Mass., presiding**  
**Discussion from the following aspects**  
**Relation of Personal Qualities and Attitudes to Successful Hospital Administration. G. HARVEY ACNEW, M.D., Toronto, Ont.**  
**Critical Analysis of Present Methods of Training for Hospital Administration. L. M. BILSTONE, M.D., New York**  
**General Discussion. Opened by GERRARD HARTMAN, Chicago**

**Tuesday, 9:30 a.m. — Savoy Room, Copley-Plaza Hotel**  
**Panel Discussion. Essentials Pertaining to an Efficient Obstetrical Department in the Hospital. HARVEY B. MATTHEWS, M.D., Brooklyn, leader. Collaborators: JORN K. FRASER, M.D., Montreal; JOSEPH L. BAER, M.D., Chicago; JAMES R. MILLER, M.D., Hartford, M.D., Chicago; JAMES R. JERSEY, City, N.J.**  
**Topics for discussion. Accommodations, facilities and equipment of a modern obstetrical department. Supervision and management of the obstetrical staff. Qualifications of the medical staff in the practice of obstetrics within the hospital. Control of the clinical work. Essentials of a complete obstetrical record. Control of infections and complications. Periodic analytical summaries of end results. Care of the newborn. Graduate training in obstetrics.**

**Tuesday, 9:30 a.m. — Sheraton Room, Copley-Plaza Hotel**  
**Panel Discussion. Essentials Pertaining to an Efficient Department of Orthopedic Surgery in the Hospital. HENRY H. KESSLER, M.D., Newark, N.J., leader. Collaborators: FRANK D. DICKSON, M.D., Kansas City, Mo.; FLEMONT A. CHANDLER, M.D., Lewiston, Maine; WILIAM B. SELTZER, New York**  
**Topics for discussion. Accommodations, facilities and equipment of a department of orthopedic surgery in a hospital. Supervision and management of the department of orthopedic surgery. Personnel — resident, medical and nursing staffs. Qualifications of the medical staff to do orthopedic surgery. Control of the**

clinical work of the department of orthopedic surgery. Essential contents of the medical record in orthopedic surgery. Review and analysis of the clinical work of the department of orthopedic surgery. Splint and brace shop. Follow-up and study of end-results. Graduate training in orthopedic surgery.

*Tuesday, 11:00 a.m.—Swiss Room, Copley-Plaza Hotel*

Panel Discussion: Organization and Functioning of the Medical Staff. JOSEPH C. DOANE, M.D., Philadelphia, leader. Collaborators: STANLEY J. SEGER, M.D., Milwaukee; JULIUS H. COMROE, York, Pa.; CHARLES B. PUESTOW, M.D., Chicago; ALLAN CRAIG, M.D., Bangor, Maine; MERRILL N. FOOTE, M.D., Brooklyn. Topics for discussion: Standards of qualifications in making appointments to the medical staff. Procedure in making appointments to the medical staff. Legal responsibility of the hospital in respect to the professional work of the hospital. Supervision and control of major surgery and major obstetrics. Basic considerations in making promotions on the medical staff of the hospital. Essential features in conducting the medical staff conference. Maintaining adequate medical records. Increasing the number of consultations in hospital practice. Supervision of the work of the resident medical staff. Responsibility of the senior members of the medical staff in instructing junior members.

*Tuesday, 11:00 a.m.—Sheraton Room, Copley-Plaza Hotel*

Panel Discussion: Essentials Pertaining to an Efficient Department of Anesthesia in the Hospital. RALPH T. KNIGHT, M.D., Minneapolis, leader. Collaborators: RALPH M. TOVELL, M.D., Hartford; HENRY RUTH, M.D., Merion, Pa.; ELEANOR F. HOWARD, M.D., Boston. Topics for discussion: Accommodations, facilities and equipment of the department of anesthesia in the hospital. Supervision and management of the department of anesthesia. Essential qualifications for the efficient administration of anesthesia. Anesthesia techniques to be maintained. A critical analysis of newer types of anesthetics and methods of administration. Hazards associated with the administration of anesthetics. Training of interns and residents in the administration of anesthetics. Follow-up and study of end-results in the administration of anesthetics. Handling of emergency anesthetics. Graduate training in anesthesiology.

*Tuesday, 2:00 p.m.—Swiss Room, Copley-Plaza Hotel*

WILSON W. KNOWLTON, M.D., Boston, presiding. The Organization of a Blood Transfusion Department in a General Hospital. LEO M. ZIMMERMAN, M.D., and SIMONE O. LEVINSON, M.D., Chicago. Organization and Use of the Medical Library by the Medical Staff and Personnel of the Hospital. L. MARGUERITE PRIME, Chicago. A Successful Plan in Handling the Personnel Health Service in the Hospital. JOSEPH G. NORBY, Milwaukee. The Control and Assignment of Duties of Non-Professional Workers in the Hospital. FRANCES C. LADD, R.N., Boston.

*Tuesday, 4:30 p.m.—Foyer, Copley-Plaza Hotel*

Consultation Service: Internships and Residencies. M. G. WESTMORELAND, M.D., Chicago. Medical Record Problems. EDNA K. HUFFMAN, R.R.L., Chicago. Medical Social Service. MABEL R. WILSON, Boston.

Medical Staff Problems. PAUL S. FERGUSON, M.D., Chicago. Sterilization of Surgical Dressings, Instruments, Rubber Goods, Supplies, etc. SAMUEL R. D. HEWITT, M.D., St. John, New Brunswick.

*Tuesday, 8:00 p.m.—Swiss Room, Copley-Plaza Hotel*

Panel Discussion: The Hospital Trustee in his Relationships and Responsibilities. RAYMOND P. SLOAN, New York, leader. Collaborators: FRANK O. ROBSON, Southbridge, Mass.; JOHN MACGREGOR, Boston; SAMUEL STEWART, Lewiston, Maine; CHARLES F. WILINSKY, M.D., Boston. Topics for discussion: Qualifications of the ideal hospital trustee. Acquiring essential knowledge concerning hospital administration. Relationship of the hospital trustee to (a) the administration; (b) the medical staff. The problem of the hospital trustee in selecting a hospital administrator. The trustee's responsibility in the increasing financial responsibility of the hospital. The legal or liability significance. Meeting the possible liability of the present demands on hospitals incident to the preparedness program. Preparation and conduct of the monthly meeting of the board of trustees. Monthly and annual reports. The trustee's participation in public relations of the hospital. Motion picture: White Battalions—Serving All Mankind.

*Wednesday, 7:45 a.m.—Salon, Copley-Plaza Hotel*

Breakfast Conference, Sponsored by the Boston Medical Record Librarians Association in co-operation with the American College of Surgeons: Forum on Fundamental Considerations in the Art and Science of Medical Record Keeping. W. FRANKLIN WOOD, M.D., Waverley, Mass., presiding. Discussion from the following aspects: A Critical Analysis of the Present Ways and Means of Training Medical Record Librarians. SISTER M. LORETTA, R.R.L., Duluth, Minn. The Place of the Medical Record Librarian in the Hospital Organization. MARGARET DuBOIS, M.D., Chicago. What the Medical Record Librarian Can Contribute Towards Making a Success of Her Career. MARGARET TAYLOR, R.R.L., Rochester, N. Y.

*Wednesday, 9:30 a.m.—Swiss Room, Copley-Plaza Hotel*

Joint Conference with American Association of Medical Record Librarians. ROBIN C. BUEKEL, M.D., Philadelphia, presiding. Our Challenge—Good Medical Records in Our Hospitals. ANNA C. SCHULZE, R.R.L., Philadelphia. The Role of the Record Librarian in the Changing World. SISTER MARY SERVATIA, R.R.L., St. Louis. The Preparation of Medical Statistics and Special Studies for the Medical Staff. MARY M. NEWTON, R.R.L., Evanston, Ill. Medical Photography as an Aid to More Comprehensive Medical Records. C. G. BROWNELL, Rochester, N. Y. Organization and System in Handling Tumor Clinic Records. FLORENCE G. BABCOCK, R.R.L., Ann Arbor, Mich. The Introduction and Orientation of the Intern to Medical Record Keeping in the Hospital. MARSHALL DAVISON, M.D., Chicago. Round Table Conference—Discussion of the following topics: The filming of medical records. The present status of the standard nomenclature. Recording of infections in the medical record. The place of the medical secretary in securing medical records. Floor supervision of current



medical records. The use of the dictaphone in securing medical records. Assisting the members of the medical staff by providing statistical and other information for scientific presentations. Co-operation between the medical record department and the medical library. Ideal setup for the medical record room. Postgraduate courses for medical record librarians.

### Wednesday, 2:30 p.m. — Local Hospitals

#### GROUP CONFERENCES AND DEMONSTRATIONS

Beth Israel Hospital **CHARLES F. WILINSKY, M.D.**, Director.

Administration, Business Methods, Hospital Accounting, and Other Activities **SAMUEL D. KATZMAN**.  
Admitting and Discharging Procedures **NATALIE H. NATHAN**.

Operating Room Organization and Management, Setup for Major Operation—Supplies, Facilities, and Personnel. **MARY C. GILMORE, R.N.**

Organization and Management of a Blood Bank. **BENJAMIN ALEXANDER, M.D.**

Boston Dispensary. (New England Medical Center). **FRANK E. WING, Director**.

Outpatient Department—Organization, Clinic Management and Control, Admitting, and Other Administrative Procedures. **EDITH R. CANTERBURY** and **KATH ARNE E. WAKEFIELD**.

Pharmacy Service—Organization, Management, and Service to Outpatients. **HAROLD E. SANDBERG**.  
Health Education in an Outpatient Department. **FRANCES STERN** and **MARY PRAFFMAN**.

Purchasing, Accounting, and Central Store Supply. **ABRAHAM E. DENES**.

Boston Lying in Hospital. **WILSON W. KNOWLTON, M.D.**, Superintendent.

Study Tour of Hospital, General Routine, Technique of Isolation of Obstetrical Patients, Identification of Infants, Care of the Premature, Technique for Maintenance of Breast Feeding, Directory for Mothers' Milk, Other Features of General Interest. **GERTRUDE GARRAN, R.N.**

Children's Hospital. **GEORGE VON L. MEYER, Director**.  
Administration of Blood and Plasma Transfusions to Infants. House officer and graduate nurse.  
Nursing Care of the Infant Surgical Patient. Nursing supervisor.

The New Arthur T. Legg Room for Functional Rehabilitation of the Handicapped, Pool and Underwater Exercises, Different Methods of Physiotherapy for Children. Physiotherapy Staff of Children's Hospital and Harvard Infantile Paralysis Committee.

Haynes Memorial Hospital, Brookline (Massachusetts Memorial Hospitals). **HELVY M. POLLOCK, M.D.**, Superintendent.

Study Tour of Contagious Hospital—Technique in the Care of Communicable Diseases. **DR. SMITH**.

Joseph H. Pratt Diagnostic Hospital (New England Medical Center). **SAMUEL PROGER, M.D.**, Medical Director.

Graduate Teaching in Medicine, Dietetics and Laboratory Methods. **SAMUEL PROGER, M.D.**

Clinical Laboratory—Organization, Management, and Service. **JOSEPH BENNETT, M.S.**

Massachusetts Eye and Ear Infirmary. **NATHANIEL W. FAXON, M.D.**, Director.

Nursing Technique for Eye, Ear, and Throat Conditions. **MARIE SCHERER, R.N.**

Bronchoscopic Clinic—Organization, Management of Patients, and Technical Procedures. **JESSIE STEWART, R.N.**

Massachusetts General Hospital. **NATHANIEL W. FAXON, M.D.**, Director.

Medical Records; Organization, Management, and Service; Complete Unit Record System, Soundex System of Filing Cards; Follow-up and Follow Results. **GENE VIVIE C. CHASE**.

Anesthesia Department: Organization, Management, and Service. **HENRY K. BECHTER, M.D.**

Diagnostic Clinic A Consultative Service for Private Patients. **T. STEWART HAMILTON, M.D.**

Massachusetts Memorial Hospitals. **HELVY M. POLLOCK, M.D.**, Superintendent.

Nursery Management, Mothers' Milk Supply, Procedure and Technique in Making Infants' Formulas. **MRS. HODGSON**.

Organization and Management of a Blood Bank. **DR. DARTON**.

Anesthesia Department—Organization, Management, and Service. **DR. FERGUSON**.

Electrocardiographic Activities in a General Hospital. **JAMES M. FALKNER, M.D.**

New England Baptist Hospital. **GEORGE M. BOLLER, Acting Superintendent**.

Operating Room Organization and Management, Setup for Major Operation—Facilities, Supplies, Personnel. **ARDIS RAUPACH**.

Air-conditioning in Operating Suite. **WALTER F. LOVERING** and **ARDIS RAUPACH**.

Special Diet—Building Special Diets on House Menu. **HELEN G. McDONALD**.

Gift Shop. **BESSIE A. WHITE**.

New England Deaconess Hospital. **REV. WARREN F. COOK, Superintendent**.

Nursing Procedure with Neurosurgical Patients. **MARJORIE B. DAVIS, R.N.**

Conducting a Profitable Pharmacy Store. **HOWARD PRINGLE**.

Social Service Procedures with Diabetic and Cancer Patients. **GERYDE S. JAMESON**.

Peter Bent Brigham Hospital. **NORBERT A. WILHELM, M.D.**, Superintendent.

Preparation of Parenteral Solutions—Technique of Administering. **CARL W. WALTER, M.D.**

Sterilization of Supplies and Instruments. **CARL W. WALTER, M.D.**

### Wednesday, 4:30 p.m. — Foyer, Copley-Plaza Hotel

Consultation Service.

Nursing Service. **MARY SHEPARD, R.N.**, Cambridge, Mass.

Obstetrical Department Management. **FRANCES YOUNG, Boston**.

Occupational Therapy. **LUCY G. MORSE, O.T.R.**, Boston.

Outpatient Department Problems. **A. G. INGLEBACH, M.D.**, Cambridge, Mass., and **SHERMAN THORNDIKE, M.D.**, Boston.

Personnel Management and Personnel Relations. **FRANK J. WALTER, Denver, Colo.**

Physical Therapy. **MARY NEWITT, Boston**.

Public Relations. **JOSEPH P. LYONS, M.D.**, Quincy, Mass.

Wednesday, 8:00 p.m. — Screen Room, Copley-Plaza Hotel.  
Motion Pictures for Hospital Personnel. How We Hear, How We See (sound), Foods and Nutrition (sound), Heart and Circulation (sound), A New Day (deals with pneumonia) (sound), Goodbye, Mr. Term, Proper Care and Use of Hypodermic Needles, White Baitalons Serving All Mankind.

*Thursday, 7:45 a.m.—Salon, Copley-Plaza Hotel*

Breakfast Conference on Hospital Public Relations.

Discussion from the following aspects:

Underlying Principles of the Public Relations Program.

Prof. MAX R. GROSSMAN, Boston.

The Written Word—Newspaper Publicity. WESLEY FULLER, Boston.

The Spoken Word—Radio Talks. DEL CASTILLO, Boston.

The Visual Way—Tours Through the Hospital and Motion Pictures.

*Thursday, 9:30 a.m.—Swiss Room, Copley-Plaza Hotel*

Panel Discussion: Essentials Pertaining to an Efficient Department of Urology in the Hospital. GEORGE F. CAHILL, M.D., New York, leader. Collaborators: LEO P. DOLAN, M.D., Toledo; GILBERT J. THOMAS, M.D., Minneapolis; GEORGE O'HANLON, M.D., Jersey City, N.J.

Topics for discussion: Accommodations, facilities and equipment of a department of urology in the hospital. Supervision and management of the department of urology. Personnel management—resident, medical and nursing staffs. Qualifications of the medical staff to do urology. Control of the clinical work of the department of urology. Essentials of the medical record in urology. Regular periodic review and analysis of the clinical work in urology. Follow-up and study of end results. Graduate training in urologic surgery.

*Thursday, 11:00 a.m.—Swiss Room, Copley-Plaza Hotel*

Panel Discussion: Essentials Pertaining to an Efficient Department of Ophthalmology and Otolaryngology in the Hospital. CONRAD BERENS, M.D., and MARVIN F. JONES, M.D., New York, leaders. Collaborator: LAWRENCE T. POST, M.D., St. Louis.

Topics for discussion: Accommodations, facilities and equipment of the department of ophthalmology and

otolaryngology. Supervision and management of the department of ophthalmology and otolaryngology. Personnel of the department of ophthalmology and otolaryngology—resident, medical and nursing staffs. Qualifications of the medical staff to do ophthalmological and otolaryngological surgery. Control of the clinical work in the department of ophthalmology and otolaryngology. Regular periodic review and analysis of the clinical work of the ophthalmological and otolaryngological department. Essentials of the medical record for ophthalmological and otolaryngological patients. Anesthetic service for the ophthalmological and otolaryngological patients. Training of interns and nurses in the ophthalmological and otolaryngological department. Graduate training in ophthalmology and otolaryngology.

*Thursday, 2:00 p.m.—Swiss Room, Copley-Plaza Hotel*

Round Table Conference: Administrative practices, policies, personnel; business methods; medical staff organization; medical staff conferences; medical records; diagnostic and therapeutic services; obstetrical, nursing, food and pharmacy services; outpatient department; housekeeping; maintenance and utilities; hospital auxiliaries; and other practical problems. ROBIN C. BUECKI, M.D., Philadelphia, and G. HARVEY AGNEW, M.D., Toronto, Ont., leaders.

Collaborators: GEORGE O'HANLON, M.D., Jersey City, N. J., SIDNEY G. DAVIDSON, New Haven, Conn.; LEWIS E. JARRETT, M.D., Richmond, Va.; E. MURIEL MCKEE, R.N., Brantford, Ont.; SISTER MARY ALPHONSUS, Teaneck, N. J.; EDNA H. NELSON, R.N., Chicago; SISTER M. PATRICIA, O.S.B., Duluth, Minn.; EDNA D. PRICE, R.N., Concord, Mass.; L. V. RAGSDALE, M.D., Grand Rapids, Mich.; HELEN ROBINSON, R.N., Wauseon, Ohio; DAN TRAINER, Lynn, Mass.; FRANK J. WALTER, Denver.

# PRELIMINARY CLINICAL PROGRAM

## GENERAL SURGERY

Monday

### BOSTON CITY HOSPITAL

- Staff—2 Symposium Vascular disease.  
S J G NOWAK—2 Experimental hypertension  
F. A. EDWARDS—2:30. Thrombophlebitis in unusual forms  
E. L. O'NEIL—3 Lumbar sympathectomy for vascular disease  
D. C. GOLDFARB—3:30. False aneurysm of femoral artery.  
T. LEARY—4 Pathological aspects of vascular disease  
E. E. O'NEIL—4:30 Refrigeration in gangrene of lower extremities.

### COLLIS P. HUNTINGTON MEMORIAL HOSPITAL

- Staff—2 15. Dry clinic.  
JOSEPH C. ALB Recent advances in our knowledge of bone diseases  
CHANNING C. SIMMONS Malignant tumors of bone  
RICHARD DRESSER Radiographic demonstration of bone tumors and certain rare forms of skeletal disease  
CHARLES E. DUNLAP Carcinogenic agents  
CLIFFORD C. FRANSEEN Industrial cancer

### MASSACHUSETTS GENERAL HOSPITAL

- H K. BEECHER and associates—2 Dry clinic Anesthesia and related subjects  
H K. BEECHER—2 Use of ether in the presence of pulmonary tuberculosis, anesthesia for transpleural gastric surgery  
JULIA G. ARROWOOD—2:25 Fractional spinal anesthesia  
H K. BEECHER—2:35 Anesthesia and shock  
Staff—3 10 Discussion  
FOWARD B. BENEDICT—3 30 Endoscopy, bronchoscopy and esophagoscopy with special emphasis on the two newer endoscopic methods, gastroscopy and patients oscopy, demonstration with lantern slides and patients  
Staff—2. Symposium Peripheral vascular disease, varicose veins and their complications  
H H FAXON—2 Fundamental considerations, anatomy, physiology, etiology, examination  
R H THOMPSON—2 15 Late results following treatment of uncomplicated varicose veins  
H H FAXON—2 30 Present concept of treatment  
R R LINTON—2 45 Chronic and recurrent ulceration of lower extremities, etiological factors and classification, present concept of treatment  
Staff—3 30 Discussion  
H H FAXON, R H THOMPSON, and R R LINTON 4  
Operations R H THOMPSON and associates—2 Dry clinic Tumors  
L M DALAND, A O HAMPTON and associates—2 Roentgen diagnosis of cancer of the lung  
G W HOLMES—2 15 Roentgen treatment of cancer of the lung  
J V MEIER—2 30 Changing concepts in the treatment of cancer of the cervix  
L M DALAND—2 45 The locus of recurrence in cancer of the breast  
R. SCHATTNER—3 End results of roentgen therapy in cancer of the larynx.

- L L. ROBBINS—3:15 The treatment of polycythemia vera by spray radiation  
T B MALLORY—3 30 Malignant ulcers of the stomach  
C L. WILCH—3 45 Gastric ulcers in relation to gastric cancer  
J R. LINGLEY—4 Comparison of skin effect on the albino rat of 200 k v and 1200 k v. roentgen ray  
G W TAYLOR—4 15 The value of regional dissection in cancer cases

### NEW ENGLAND BAPTIST HOSPITAL

- H D ADAMS and N W SWINTON—1 30 Operative clinic  
Thyroid, stomach, colon, rectum and biliary tract  
U H EVERSOLE, LEO V HAND, and M J NICHOLSON—1 30 Demonstrations Anesthesia

### NEW ENGLAND DEACONESS HOSPITAL

- H D ADAMS and N W SWINTON—1 30 Operative clinic  
Thyroid stomach colon, rectum, and biliary tract  
U H EVERSOLE, LEO V HAND, and M J NICHOLSON—1 30 Dry clinic Anesthesia in thyroid surgery, including intratracheal anesthesia, pre-operative and post operative medication, recent developments in spinal anesthesia  
CARL SOUDERS Postoperative pulmonary complications  
JAMES EVANS Thrombophlebitis and pulmonary embolism

### NEW ENGLAND MEDICAL CENTER

(Joseph H Pratt Diagnostic Hospital)

- Staff—2 Dry clinic  
JOSEPH H PRATT—2 Value of secretin test in diagnosis of pancreatic disease  
WILLIAM DAMESHEK—2 30 Indications for splenectomy, case reports  
JOHN D. ADAMS—3 Various conditions found in the hip joint following injury  
EDWARD L. YOUNG—3 30 Peritoneoscopy

### PALMER MEMORIAL HOSPITAL

- Staff—2 Symposium Carcinoma of the breast  
CLIFFORD C. FRANSEEN Find results of surgical treatment  
L. S. MCKITTRICK Interstitial irradiation treatment of carcinoma of the breast with platinum radium needles  
J H MARKS X ray therapy of carcinoma of the breast  
SHIRLEY WARRIN Relation between chronic cystic mastitis and carcinoma of the breast

Tuesday

### BETH ISRAEL HOSPITAL

- Staff 9 Dry clinic  
ARNOLD SPARK Biliary tract disease left sided pain  
C G MIXTER Technique of immediate cholangiography motion pictures  
L A HIRSHMAN Cholangiography, indications for and end results  
H A FRANK Advantages of intravenous synthetic vitamin K<sub>1</sub> over other vitamin K preparations  
A M SELIGMAN Vitamin P in capillary fragility  
Staff—10 10. Operative clinic  
C G MIXTER Cholecystectomy and cholangiography.

- JACOB FINE. Cholecystectomy, transverse incision.  
 L. H. NASON. Peritoneoscopy, spinal anesthesia.  
 ARNOLD STARR. Peritoneoscopy, local anesthesia.  
 Staff—2. Dry clinic:  
 MAX DAVIS. Ovarian tumors with endocrine effects.  
 R. B. DAVIDOFF. Relationship of cystic disease of the breast to disease of the uterus and adnexa.  
 L. A. HERMANSON. Comparative merits of the vaginal smear and endometrial biopsy in diagnosis of ovarian function.  
 S. L. CARGILL. Hyperparathyroidism.  
 D. D. BERLIN. Carcinoma of the thyroid.  
 M. F. LESSES. Complications of thyroid surgery.  
 S. L. CARGILL. Management of recurrent and persistent thyrotoxicosis.  
 D. D. BERLIN. The avoidance of complications in thyroid surgery.

*Scientific Exhibit—Daily*

- JOSEPH GOODMAN. Pathogenic fungi in foot infections.  
 H. F. FRIEDMAN. Malignant disease before and after treatment by radiation.  
 ABRAHAM RUDY and S. R. MUELLNER. Neurogenic bladder in diabetes mellitus.  
 JULIUS LOMAN. Action of autonomic drugs on the gastro-intestinal and genito-urinary tracts.  
 S. A. ROBINS. Urethrography and cystography.  
 W. S. ALTMAN and L. A. HERMANSON. Cholangiography.  
 LEONARD NATHAN and KURT THOMA. Cysts and tumors of mouth and jaw.  
 JULIUS LOMAN. Cerebral arteriography.  
 ARNOLD STARR and H. A. FRANK. Venography in deep phlebitis of lower leg.  
 S. S. HANFLIG. Mechanical device for reduction of Colles' fracture.

BOSTON CITY HOSPITAL

- Staff—2. Dry clinic: Gastric lesions.  
 W. R. MORRISON—2. Gastrojejunocolonic fistula.  
 C. W. MCCLURE—2:30. Gastroscopy, kodachrome pictures.  
 A. R. KIMPTON—3. Cancer of stomach.  
 W. R. MORRISON—3:30. Perforated peptic ulcer.  
 E. E. O'NEIL—4. Transpleural approach for carcinoma of upper end of stomach.  
 T. W. WICKHAM—4:30. Cholecystitis and its relation to peptic ulcer. Review of six hundred cholecystectomies.

PETER BENT BRIGHAM HOSPITAL

- ELLIOTT C. CUTLER and ROBERT E. GROSS—9. Operations: Ligation of patent ductus arteriosus; pericardiectomy.  
 ELLIOTT C. CUTLER and associates—10. Symposium: Surgery of the heart and blood vessels.  
 C. SIDNEY BURWELL. Forms of heart disease amenable to surgery.  
 SAMUEL A. LEVINE. Cardiac disease simulating surgical conditions of the abdomen and vice versa.  
 EUGENE C. EPPINGER. Indications for surgery for patent ductus arteriosus.  
 ROBERT E. GROSS. Surgical treatment of patent ductus arteriosus.  
 ELLIOTT C. CUTLER. The technique of pericardiectomy.  
 MERRILL C. SOSMAN. The rôle of the roentgenologist in cardiac surgery.  
 JOHN HOMANS. Peripheral vascular disease.  
 MARSHALL N. FULTON. Angioma of skeletal muscle.  
 DAVID CHEEVER—2. Demonstration: Surgical anatomy of the abdomen.

CHILDREN'S HOSPITAL

- WILLIAM E. LADD and associates—10:30. Dry clinic: Diseases of the gastro-intestinal tract in childhood, followed by questions and discussion.  
 WILLIAM E. LADD. Atresia, stenosis, and malrotation.  
 THOMAS H. LANMAN. Pyloric stenosis.  
 ROBERT E. GROSS. Intussusception.  
 HENRY W. HUDSON, JR. Appendicitis.

MASSACHUSETTS GENERAL HOSPITAL

- A. W. ALLEN and associates—8. Symposium: Gastric lesions.  
 C. M. JONES—8. Medical considerations.  
 A. O. HAMPTON and associates—8:30. Roentgenological studies.  
 E. B. BENEDICT—8:50. Gastroscopy and peritoneoscopy.  
 C. E. WELCH—9:10. Gastric ulcer.  
 LANGDON PARSONS—9:30. Cancer of the stomach.  
 R. H. SWEET—9:50. Transthoracic gastrectomy.  
 A. W. ALLEN—10:10. Surgical procedures for gastric lesions.  
 Staff—10:30. Operations: Gastric resections for benign and malignant lesions.  
 H. H. FAXON, HORATIO ROGERS, and associates—9. Symposium: Acute appendicitis.  
 HORATIO ROGERS. Present status; chief factors in present mortality rates, late diagnosis and/or treatment, faulty appraisal of individual patients, rigid policies of treatment, faulty technique, type of incision.  
 W. D. SMITH. Appendicitis in general medical practice.  
 HORATIO ROGERS. Appendiceal peritonitis before localization.  
 H. H. FAXON. Appendiceal peritonitis after localization.  
 CHAMP LYONS. The rôle of bacteriology and chemotherapy in appendicitis.  
 R. R. LINTON. Special aspects of appendicitis in young children.  
 Staff—11. Operative clinic.  
 L. S. MCKITTRICK and associates—2. Symposium: Surgery of the colon and rectum.  
 L. S. MCKITTRICK—2. Operations for carcinoma of the rectum and their indications.  
 A. W. ALLEN—2:20. The management of carcinoma of the colon.  
 E. P. HAYDEN—2:40. The complications of diverticulitis of the sigmoid and their management.  
 ROY E. MABREY—3. The operative and non-operative management of internal hemorrhoids.  
 Staff—3:20. Discussion.  
 Staff—3:40. Operative clinic.  
 CHAMP LYONS and FRANK L. MELENEY (New York)—3. Dry clinic: Surgical infections.

MASSACHUSETTS MEMORIAL HOSPITALS

- HOWARD M. CLUTE, CLIFFORD D. HARVEY, CHARLES SZIKLAS, FRANK E. BARTON, and HOLLIS L. ALBRIGHT—8. Operative clinic: Thyroid, gall-bladder, stomach, and colon.  
 ELEANOR FERGUSON, REGINALD HUNT, and M. JEAN BLACK. Demonstrations: Anesthesia.  
 Staff—10. Symposium: Management of blood-bank.  
 FRANK E. BARTON. Management of a blood-bank in a small hospital.  
 CHARLES BRANCH. Correlation of the hospital laboratory with the blood-bank.  
 JOHN SCUDDER (New York). Studies in treatment of shock with plasma and serum.  
 CORNELIUS P. RHOADS (New York). Present application and future development of blood substitute therapy.

- PHILLIPS L. BOND—10 Dry clinic. Lymphogranuloma venereum with rectal involvement.  
 FRANK E. BARTON—2. Demonstration of transfusion service.  
 Staff—2. Symposium: Surgery of the biliary tract.  
 KNOWLES LAWRENCE—2. Intrinsic disease of the liver simulating cholecystitis.  
 HOLLIS L. ALBRIGHT—2 20 Non-calculous gall bladder.  
 THOMAS J. ANGLEW—2 40 Complications of common duct surgery.  
 FRANK INGELFINGER—3 Duodenal drainage in diagnosis of biliary tract disease.  
 CHESTER KEEFER—3 20 Liver abscess as a cause of prolonged fever.  
 HOWARD M. CLUTE—3 40 Stricture of the bile ducts

#### NEW ENGLAND BAPTIST HOSPITAL

- F. H. LAHEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCLOCK—9. Operative clinic: Thyroid, stomach, colon, and biliary tract.  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—9. Anesthesia demonstrations: Regional, spinal, continuous spinal, and general.  
 H. D. ADAMS and N. W. SWINTON—1 30 Operative clinic: Thyroid, stomach, colon, rectum, and biliary tract.  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1 30. Demonstrations: Anesthesia

#### NEW ENGLAND DEACONESS HOSPITAL

- F. H. LAHEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCLOCK—9. Operative clinic: Thyroid, stomach, colon, and biliary tract.  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—9. Anesthesia demonstrations: Regional, spinal, continuous spinal, and general.  
 H. D. ADAMS and N. W. SWINTON—1 30 Operative clinic: Thyroid, stomach, colon, rectum, and biliary tract.  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1 30. Demonstrations: Anesthesia.  
 F. H. LAHEY, LEWIS M. HERTHAL, ELMER C. BARTELS, and H. J. PERKINS—2. Symposium: Thyroid surgery. Subtotal thyroidectomy, diagnosis of hyperthyroidism, diagnosis and treatment of the thyrocardiac, complications following thyroid surgery, recent developments in blood iodine studies.

#### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

- ELEANOR E. COWAN—10 Out patient clinics: Gynecological, medical, and pediatric.  
 G. LYNET MILLER—10 Pathological presentation: Carcinoid tumor of small intestine, metastases to liver, carcinoma of gastro-intestinal tract.  
 RACHEL L. HARDWICK, DIANCA R. LEE, and MERRY L. FITTMAN—3 Dry clinic: Correlation of electroretinocardiography with roentgenography in rheumatic heart disease, congenital heart disease, and functional abnormalities, with presentation of cases.

#### NEW ENGLAND MEDICAL CENTER

(Joseph H. Pratt Diagnostic Hospital)

- Staff—2. Dry clinic.  
 EDWARD T. WHITNEY—3 Bleeding per ano, illustrated with lantern slides.  
 C. H. LAWRENCE—2 30 Masculinizing factors in the female.  
 K. S. ANDREWS, HENRY H. LERNER, and WILLIAM M. SHEDDEN—3 30. Recent advances in diagnosis and treatment of cancer of the stomach.

#### PONDVILLE HOSPITAL

- E. M. DALAND, G. W. TAYLOR, H. ROGERS, T. J. ANGLEW, R. H. WALLACE, and associates—9. Operative clinic: Cancer.  
 Staff—11. Dry clinic:  
 E. M. DALAND End results in cancer of the breast.  
 T. J. ANGLEW Cancer of the mouth, demonstration of cases.  
 G. W. TAYLOR Lymph node metastases.  
 S. WARREN and associates. Pathological demonstration.  
 C. L. DEWAS and associates Roentgen demonstration of bone tumors.

#### ST. ELIZABETH'S HOSPITAL

- Staff—9. Operative and dry clinic:  
 JOSEPH STANTON—9 Thyroidectomy.  
 MICHAEL E. MCGARTY—9 Bilateral recurrent inguinal hernia.  
 JOSEPH STANTON—10 Biliary tract operation.  
 FRANCIS JANZEN—10 30 Discussion of sub-deltoid bursitis and ruptured supraspinatus tendon.  
 WILLIAM F. DOLAN—11. Wrist injuries in industry.  
 MICHAEL E. MCGARTY—11 30. Skin grafts, demonstration of cases.

#### SALLM HOSPITAL

- W. G. PHIPPS, DONALD A. NICKERSON, and S. A. WILSON—10. Dry clinic: Uses and abuses of laboratory and roentgenological procedures in abdominal surgery.  
 L. L. PETERSON—11 Prostatic surgery with some newer methods of diagnostic approach.

#### UNITED STATES MARINE HOSPITAL

- RICHEY L. WALCH and associates—8 Operative clinic: Hernioplasty, indirect, direct, and femoral, appendectomy, ligation of saphenous vein, hemorrhoidectomy.  
 RICHEY L. WALCH and associates—1 Dry clinic:  
 JAMES I. SPINDLER Parasitic appendicitis.  
 KENNETH HAINFIELD Femoral hernia, a simple operation with report of cases.  
 RICHEY L. WALCH Terminal ileitis.  
 JOHN A. PRIOR Rupture of spleen, delayed hemorrhage.

#### UNITED STATES NAVAL HOSPITAL

- J. J. A. McMillen and staff—9. Operations.

Wednesday

#### BETH ISRAEL HOSPITAL

- Staff—9. Dry clinic:  
 L. H. NASON Pressure treatment of keloids.  
 J. B. SEARS Prophylaxis of pulmonary embolism by division of femoral vein.  
 EDWARD HIRSCH Changes in volume of the peritoneal cavity following intercostal nerve paralysis.  
 C. G. MIXTER Giant hernia.  
 ARNOLD STARR Advanced regional ileitis.  
 C. G. MIXTER Transverse ileocolostomy with or without resection for regional ileitis.  
 Staff—10 30 Operative clinic.  
 C. G. MIXTER Intestinal resection.  
 J. B. SEARS Division of femoral vein for treatment of non fatal pulmonary embolus.  
 D. D. BERLIN Thyroidectomy.  
 Staff—2 Dry clinic:  
 M. D. ALTMAN Obstruction of superior vena cava.  
 BENJAMIN ALFANDER Blood bank.  
 MAX HAYES and SAMUEL GILMAN Venous pressure changes in lower extremities during and after abdominal surgery.

- S. B. BEASER. Rare earth anticoagulants.  
 JACOB FINE. Thrombophlebitis and embolism, diagnostic and therapeutic considerations.  
 BENJAMIN ALEXANDER. Polycythemia vera in peripheral vascular disease.  
 B. F. MASSELL and S. B. BEASER. Evaluation of therapy of peripheral vascular disease.  
 JACOB FINE. Adrenal cortical hormones in shock and hemorrhage.

## BOSTON CITY HOSPITAL

## Staff—9. Symposium: Cancer.

- Department of Pathology—9. Splenogenic myeloid metaplasia; argentophil tumors (carcinoid).  
 DR. JOLIFF—9:30. Surgical treatment of myeloma.  
 F. W. O'BRIEN—9:50. Cancer and x-ray therapy.  
 E. A. COONEY—10:20. Carcinoma of breast.  
 A. R. KIMPTON—10:45. Cancer of large intestine.  
 CHARLES C. LUND—11:10. Cancer of mouth.  
 WILLIAM MORRISON—11:35. Cancer of stomach.

## Staff—2. Symposium: Thyroid disease.

- R. C. COCHRANE—2. Tumors of parathyroid, lantern slides.  
 D. D. BERLIN—2:30. Hyperthyroidism in cancer of thyroid.  
 W. T. SALTER—2:50. Graves' disease without hypertension.  
 RICHARD SMITH—3:10. Adenoma of thyroid.  
 Staff—2. Dry clinic:  
 GORDON M. MORRISON—2. Radial nerve injury with fracture of humerus.  
 J. EDWARD FLYNN—2:30. Anatomical and clinical investigations of deep fascial space abscess of hand.  
 T. K. RICHARDS—3:15. Traumatic injuries of the knee joint.  
 A. P. AITKEN—3:45. Epiphyseal separation.  
 ROBERT ULIN—4:30. Clubfeet.

## Staff—3:30. Symposium: Vitamins in surgery.

- CHARLES C. LUND and J. H. CRANDON—3:30. Vitamin C and wound healing.  
 WALTER WEGNER and MERRILL MOORE—4:15. Vitamins in presence of head injuries.  
 DR. MIKELJOHN—4:45. Presentation of cases.

## PETER BENT BRIGHAM HOSPITAL

- ELLIOTT C. CUTLER and ROBERT ZOLLINGER—9. Operations: Gastric resections.  
 ELLIOTT C. CUTLER and associates—10. Symposium: Gastric and duodenal ulcer.  
 ELLIOTT C. CUTLER. Indications for surgery.  
 EDWARD S. EMERY, JR. Medical management of bleeding peptic ulcer.  
 MERRILL C. SOSMAN. Significance of prepyloric ulcer.  
 HARRY A. WARREN. Duodenal diverticulum.  
 ROBERT ZOLLINGER. Surgical treatment of severe duodenal ulcer.  
 ELLIOTT C. CUTLER. Results of acute gastroduodenal perforation.  
 CARL W. WALTER—2. Symposium: Aseptic technique.

## CARNEY HOSPITAL

- A. McK. FRASER, WILLIAM E. BROWNE, and staff—9. Operative clinic: Gastro-intestinal, biliary tract, thyroid and hand.  
 Staff—2. Dry clinic:  
 WILLIAM E. BROWNE. Moving picture demonstration and brief description of unusual lesions of arm, forearm, and hand, showing condition present before treatment and end-results. Cases will include xanthomata, glomus tumor, so-called trigger finger contract

tures, aneurysms in hand, melanotic carcinoma, tendon suture repair with transplanted segment of vein for covering at site of anastomosis, difference between real and pseudo-neuromata in amputation stumps, ulnar nerve repair, series of median nerve cases, results in a series of cases following radical operation for relief of Dupuytren's contracture with 90 to 100 per cent return of normal function of the hand.

DAVID C. DITMORE. Vital tissue staining, its practical application in office and hospital proctology, with report of results in a series of 1000 private patients.

W. R. MACAUSLAND. Fracture and dislocation of carpal-semilunar bones.

HAROLD G. LEE. End-results in lumbosacral fusion; end-results of epicondylar fractures of humerus.

A. LEO BRETT. Case presentation of myeloma of 12 years' duration with complete absorption of tenth vertebra.

JOHN L. DOHERTY. A simple method of treating fractures of surgical neck of humerus.

WILLIAM C. MALONEY. Practical application of clinical laboratory procedures in jaundice.

A. McK. FRASER. End-results of gall-bladder surgery.

## CHILDREN'S HOSPITAL

WILLIAM E. LADD and associates—9. Operations.

## DILLON FIELD HOUSE

(Soldiers' Field, Allston)

AUGUSTUS THORNDIKE, JR., and associates—3. Dry clinic: Athletic injuries. Summary of recent developments in the physiology of physical fatigue.

## FAULKNER HOSPITAL

## Staff—8. Operative and dry clinic:

- E. L. YOUNG, A. R. KIMPTON, F. G. BALCH, H. K. SOWLES, R. F. SHELDON, E. E. O'NEIL, R. S. TITUS, and R. J. HEFFERNAN. Operations.  
 S. C. WIGGIN. Anesthesia exhibits.  
 J. B. HAZARD. Pathological specimens, gross and microscopic.

## Staff—2. Operative and dry clinic:

- A. R. KIMPTON—2. Gastric resection.  
 H. K. SOWLES—2:15. Reconstruction operation for hypertrophied breast.  
 E. L. YOUNG—2:30. Stricture of papilla of Vater.  
 R. C. COCHRANE—2:45. Parathyroid tumors.  
 WM. C. QUINBY—3. Importance of water balance in diseases of the prostate.  
 E. E. O'NEIL—3:15. Prevention of pulmonary embolism by ligation and division of femoral vein.  
 R. F. SHELDON—3:30. Local infiltration anesthesia for pelvic delivery.  
 R. J. HEFFERNAN—3:45. Use of progesterin in treatment of habitual and threatened abortion.  
 DR. MALONEY—4. Management of bleeding in jaundice.  
 R. S. TITUS—4:15. Diabetes in pregnancy.  
 DR. STRAUSS—4:30. Importance of vitamins.  
 S. C. WIGGIN—4:45. Anesthesia for complicated surgical cases.

## MALDEN HOSPITAL

- LOUIS E. PHANEUF—9. Operation: Vaginal hysterectomy.  
 IRVING J. WALKER—9. Operation: Cholecystectomy.  
 Staff—10. Dry clinic and demonstrations:  
 GORDON D. ATKINSON—10. Urology.  
 RUSSELL F. SULLIVAN—11. Orthopedic surgery.  
 LOUIS E. PHANEUF—11:30. Gynecology.  
 IRVING J. WALKER—12. Ludwig's angina.  
 J. S. ROONEY—12:30. Pathology.  
 KENNETH K. DAY—1. Blood bank.

## Staff—2 Operative clinic

- GORDON D ATKINSON—2 Nephrectomy.  
N. A. GALLAGHER—2 30 Hysterectomy  
RUSSELL F. SULLIVAN—3 30 Spinal fusion (Hibbs')

## MASSACHUSETTS GENERAL HOSPITAL

- L. S. MCKITTRICK and associates—9 Operative and dry clinic Ulcerative colitis.  
C M JONES—9 Medical aspects, diagnosis and treatment.  
L S MCKITTRICK—9 20 Surgical aspects, types of operations and indications  
J D STEWART—9 40 Ileostomy, operative technique, postoperative complications  
RICHARD WARREN—10 10 Late results after ileostomy, social and economic aspects  
L S MCKITTRICK—10 30 Colectomy, indications, technique and results  
Staff—10 45 Discussion  
Staff—51 Operations  
H C MARBLE and associates—9 Dry clinic Surgical conditions of the hand  
H C MARBLE. Anatomy and examination  
F G. BALCH, JR. Hand tumors  
EDWARD HAMLIN, JR. Injuries to nerves of upper extremity  
BRADFORD CANNON. Skin grafts of hand  
A L. WATKINS. Physiotherapy in reconstruction  
A W REGGIO. Occupational therapy in reconstruction  
H C MARBLE. Surgical reconstruction  
A W ALLEN and associates—2 Symposium Diseases of the gall bladder and bile ducts  
A W ALLEN—2 Technical considerations of the gall bladder and bile ducts with special reference to morbidity and mortality  
RICHARD WALLACE—2 30 Acute cholecystitis  
J D STEWART—2 50 Obstructive jaundice, liver function, preparation of the patient and after-care  
RICHARD WARREN—3 15 Carcinoma of the gall bladder  
Staff—3 10 Operative clinic Extrahepatic biliary tract  
Staff—2 Symposium Peripheral vascular clinic, obliterative arterial disease  
L S MCKITTRICK—2 Fundamental considerations, classification, differential diagnosis  
EDWARD HAMLIN, JR.—2 15 Thrombo-angitis obliterans. Outline of treatment, nerve crushing, mechanical aids, indications for amputation  
H F KENNARD—2 35 Thrombo-angitis obliterans. End result study with particular reference to the economic aspect of the disease  
RICHARD WARREN—2 35 Arteriosclerotic gangrene with and without diabetes, indications for and technique of minor amputation  
T C PRATT—3 10 Arteriosclerotic gangrene with and without diabetes, indications for and technique of supracondylar amputation  
R H SMITHWICK—3 30 Lumbar sympathectomy, its role in the treatment of obliterative disease, indications for operation and operative technique  
Staff—3 50 Discussion  
Staff—4 Operative clinic Supracondylar amputation for gangrene, nerve crushing for relief of pain, lumbar sympathectomy

## MASSACHUSETTS MEMORIAL HOSPITALS

- HOWARD M CLUTE, CLIFFORD D HARVEY, CHARLES SZILAS, FRANK E BARTON, and HOLLY L ALBRIGHT—8 Operative clinic Thyroid, gall bladder, stomach, and colon

- ELEANOR FERGUSON, REGINALD MCNT, and M. JEAN BLACK. Demonstrations Anesthesia  
GEORGE LEVENE and LEON G WISSING—9 30 Demonstration X ray examination of the rectum and sigmoid with special reference to lateral view  
Staff—10 Symposium Gastric surgery  
HOWARD M CLUTE. Gastric hemorrhage  
JOHN SPRAGUE. End result studies after gastroduodenostomy  
FRANK E BARTON. Miller-Abbott tube in gastrointestinal diagnosis  
THOMAS J ANGLEM. Cancer of the stomach  
ELEANOR FERGUSON. Anesthesia for upper abdominal surgery  
FRANK E BARTON—2 Demonstration of transfusion service

## NTW ENGLAND BAPTIST HOSPITAL

- F H LAHEY, R B CATTELL, S F MARSHALL, and B P COLCOCK—9 Operative clinic Thyroid, stomach, colon, and biliary tract  
U H EVERSOLE, LEO V HAND, and M J NICHOLSON—9 Anesthesia demonstrations Regional, spinal, continuous spinal, and general  
H D ADAMS and N W SWINTON—1 30 Operative clinic Thyroid, stomach, colon, rectum, and biliary tract  
U H EVERSOLE, LEO V HAND, and M J NICHOLSON—1 30 Demonstrations Anesthesia

## NEW ENGLAND DEACONESS HOSPITAL

- F H LAHEY, R B CATTELL, S F MARSHALL, and B P COLCOCK—9 Operative clinic Thyroid, stomach, colon, and biliary tract  
U H EVERSOLE, LEO V HAND, and M J NICHOLSON—9 Anesthesia demonstrations Regional, spinal, continuous spinal, and general  
H D ADAMS and N W SWINTON—1 30 Operative clinic Thyroid, stomach, colon, rectum, and biliary tract  
U H EVERSOLE, LEO V HAND, and M J NICHOLSON—1 30 Demonstrations Anesthesia  
R B CATTELL, N W SWINTON, and EVERETT D KEITER—2 Dry clinic Diagnosis and treatment of carcinoma of rectum, rectal surgery for benign lesions, diagnosis and treatment of ulcerative colitis  
JOHN NORCROSS. Vitaminosis and recent developments in intravenous use of heparin

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

- Staff—10 Out patient clinics Gynecological, skin and allergy, pediatric and well baby  
G LINDA MILLER—10 Pathological demonstration Breast cancer

## NTW ENGLAND MEDICAL CENTER

(Joseph H Pratt Diagnostic Hospital)

- Staff—9 Dry clinic  
RICHARD H OVERNOLT—9 The operability of primary carcinoma of the lung  
KEEVE H BETTS—9 30 The management of acute pulmonary abscess  
H F MACMAHON—10 Gastric lesions in malignant hypertension  
S J THANNHARTER—10 10 Liver function tests as an aid to gall bladder surgery

## NEWTON HOSPITAL

- Staff—9 Operative clinics  
G KENNETH COOZE—9 A new arthroplasty of the hip  
LOUIS PILCHER—9 Appendectomy

- R. I. SMITH—9:30. Thyroidectomy for hyperthyroidism.  
 M. P. BRACKETT—9:30. Cholecystectomy.  
 D. G. NUTTER—10. Hysterectomy for fibroids.  
 E. D. LEONARD—10. Breast amputation.  
 HERBERT DUNPHY—11. Skin graft.  
 Staff—2. Dry clinic.  
 G. K. COONSE. Diagnosis and treatment of shoulder injuries.  
 R. I. SMITH. Tumors of the neck.  
 G. D. NUTTER. New apparatus for fractures of the clavicle.  
 CHARLES LAMB. Peripheral vascular clinic.  
 H. G. DUNPHY. Management of cicatricial contractures due to burns, skin grafting in general.  
 E. D. LEONARD. Arterial thrombosis in a young girl.

#### ST. ELIZABETH'S HOSPITAL

- Staff—9. Operative and dry clinics:  
 JOHN W. SPELLMAN—9. Surgery of the breast.  
 JOSEPH STANTON—9. Gastric surgery.  
 EDWARD M. HODGKINS—9. Herniorrhaphy, fascial strips.  
 LAWRENCE J. LOUIS—10. Cholecystectomy.  
 JOHN G. DOWNING—11. Surgical complications due to fungi. Colored motion picture, "A Clinical and Laboratory Study of Fungus Diseases."  
 JOHN W. SPELLMAN—11. Treatment of advanced cancer, demonstration of cases.  
 WILLIAM NOONAN—11:45. Spinal anesthesia.

#### UNITED STATES NAVAL HOSPITAL

- LAWRENCE J. MCCARTHY and staff—9. Operations.  
 JOHN R. MARSHALL and CHARLES H. SWAN—9. Dry clinic: Circulatory diseases of the extremities, case histories.

#### Thursday

#### BETH ISRAEL HOSPITAL

- Staff—9. Dry clinic:  
 S. S. HANFLIG. Use of traction in treatment of cervical arthritis.  
 MYER KARP. Treatment of acute subdeltoid bursitis by needling, novocain and irrigation; mechanics of fracture of surgical neck of humerus, methods of reduction.  
 M. H. ROGERS. Manipulation for chronic adhesive bursitis.  
 ARMIN KLEIN. Chemotherapy of acute sepsis of bones and joints.  
 W. S. ALTMAN. Delayed roentgenological evidence of fracture.  
 ARMIN KLEIN. Intervertebral disc, orthopedic aspects.  
 W. JASON MIXTER. Intervertebral disc, neurological and surgical aspects.  
 DAVID AYMAN. Results of sympathectomy for hypertension.  
 Staff—10:30. Operative clinic:  
 R. H. SMITHWICK. Sympathectomy for hypertension.  
 W. JASON MIXTER. Removal of intervertebral disc.  
 M. H. ROGERS. Arthroscopy of shoulder joint.  
 Staff—2. Dry clinic:  
 ALFRED HURWITZ. Sulfanilamide vs. zinc peroxide in the treatment of phagedenic ulcer.  
 LOUIS ZETZEL. The Miller-Abbott tube.  
 M. D. ALTSCHULE. Effect of abdominal surgery on respiratory dynamics.  
 H. L. BLUMGART. The surgical risk in cardiac patients.  
 JACOB FINE. Treatment of intestinal distention by sulfaguanidine.  
 ARNOLD STARR. Sulfaguanidine for the sterilization of isolated loops of colon.

#### BEVERLY HOSPITAL

- Staff—2. Dry clinic:  
 PEER P. JOHNSON. Acute pancreatic disease, its diagnosis and treatment.  
 BARNARD P. TODD. Adenoma of the islets of Langerhans.  
 RICHARD E. ALT. Abdominal manifestations of renal disease.  
 PEER P. JOHNSON and HAMMOND J. DUGAN. Results of deferred operation in acute perforated appendicitis.  
 JOSEPH A. CUNNINGHAM. A clinicopathological study of abdominal Hodgkin's disease.

#### BOSTON CITY HOSPITAL

- OTTO J. HERMANN and associates—9. Symposium: Low back pain.  
 OTTO J. HERMANN—9. Introduction.  
 JOHN T. WILLIAMS—9. Gynecological aspects.  
 AUGUSTUS RILEY—9:15. Genito-urinary aspects.  
 ROBERT ULIN—9:30. A rational method of routine back examination based on anatomical and physiological factors.  
 JOSEPH SHORTELL—9:45. Low back pain with negative x-ray, lumbosacral; sacro-iliac myositis; myositis fascitis, industrial postural, mechanical findings.  
 THOMAS H. PETERSON—10. Coccygodynia fracture of coccyx, conservation vs. surgery in treatment.  
 RUSSELL SULLIVAN—10:15. Anatomical abnormalities of fifth lumbar vertebra and lumbosacral joint.  
 G. KENNETH COONSE—10:30. Spondylolisthesis, pathology, diagnostic points, rôle of trauma in its production and treatment.  
 A. P. AITKEN—10:45. Fascial contractions.  
 MARK H. ROGERS—11. Intervertebral disc problem, orthopedic aspect.  
 P. F. BUTLER—11:15. Intervertebral disc problem, x-ray aspect.  
 DONALD MUNRO—11:30. Intervertebral disc problem, neurological aspect.  
 Staff—2. Operative and dry clinic: Appendicitis, biliary system, and hernia.  
 P. S. FOISIE—2. Appendicitis and complications.  
 G. W. PAPAN—2:30. Incision for appendectomy in extreme obesity.  
 F. F. HENDERSON and JOHN MCGOWAN—3. Operative biliary drainage for relief of jaundice, operative care of gall-bladder patient.  
 J. J. HEPBURN—3:20. Familial hemolytic jaundice and splenectomy.  
 W. R. MORRISON—3:40. Stones of the hepatic ducts subdiaphragmatic abscess.  
 CHARLES LAMB—4. Peritoneoscopy with special reference to biliary disease.  
 RICHARD SMITH—4:20. Exteriorization of small intestines in strangulated hernia.  
 D. C. GOLDFARB—4:40. Recurrent inguinal hernia.  
 Staff—2. Symposium: Anesthesia, and abdominal surgery.  
 T. W. WICKHAM—2. Foci of infection and ulcerative colitis.  
 A. R. KIMPTON—2:15. Surgery of large intestine.  
 C. W. McCLURE—2:30. Sigmoidoscopy, kodachrome pictures.  
 FRANK MARVIN—2:45. Indications and contra-indications for various anesthetics.  
 S. C. WIGGIN—3. Spinal anesthesia.  
 G. C. MOORE—3:15. Intravenous anesthesia.  
 P. S. FOISIE—3:30. Ruptured corpus hemorrhagicum.  
 ALLEN DAVIS—3:45. Calcified cyst of spleen.  
 S. J. MADDOCK—4. High and low intestinal obstruction.  
 ALLEN DAVIS—4:20. Gun shot wounds of abdomen.  
 HALSEY B. LODER—4:40. Postoperative treatment.



## PETER BENT BRIGHAM HOSPITAL

- FRANCIS C. NEWTON and J. ENGLEBERT DUNPHY—9 Operations. Colon, rectum and anus  
 ELLIOTT C. CUTLER and associates—10 Symposium. Colon, rectum and anus  
 FRANCIS C. NEWTON. Experiences with cancer of the colon  
 J. ENGLEBERT DUNPHY. Experiences with anterior resection for cancer of the rectosigmoid  
 ANDREW W. CONTRATTO and THOMAS B. QUIGLEY. Differential diagnosis of gastritis, gastro-enteritis and appendicitis  
 MERRILL C. SOSMAN. The x-ray and large bowel surgery  
 EDWARD S. EMERY, JR. Medical diseases of the colon  
 ELLIOTT C. CUTLER. Cicatrizing enteritis

## CARNEY HOSPITAL

- A. McK. FRASER, WILLIAM E. BROWNE, and staff—9 Operative clinic. Gastro-intestinal, biliary tract, thyroid, and hand  
 Staff—2 Dry clinic  
 WILLIAM E. BROWNE. Results of thyroid surgery on a general surgical service during the past 3 years, accuracy of diagnosis and careful pre-operative preparation, types of operative procedure carried out, end-results  
 ROGER C. GRAVES. Management of prostatic obstruction  
 WESTON T. BUDDINGTON. Injuries of the ureter  
 CHARLES KICKHAM. Non-calculous obstruction of the urethral pelvic junction  
 ROBERT H. ALDRICH. English experience with war burns  
 JOHN J. TODD. Use of sulfathiazole in surgical infections  
 CHARLES A. ROBINSON. Treatment of varicose ulcer  
 TIMOTHY L. P. LYONS. Results of 3 years' study of carcinoma of the large bowel  
 EDWARD T. WHITNEY. Treatment of fissure in ano

## CHILDREN'S HOSPITAL

- WILLIAM E. LADD and associates—9 Dry clinic. Plastic surgery in children, followed by questions and discussion  
 WILLIAM E. LADD. Harelip and cleft palate  
 DONALD W. MACCOLLUM. Early and late treatment of burns  
 WILLIAM E. LADD. Hands, syndactylism, polydactylism  
 ROBERT E. GROSS. Plastic operations on the anus  
 WILLIAM E. LADD and associates—10 30 Dry clinic, followed by questions and discussions  
 THOMAS H. LANMAN. Radical treatment of chronic lung suppuration  
 ROBERT L. GROSS. Surgical treatment of patent ductus arteriosus  
 FRANC D. INGRAHAM. Subdural hematoma, brain tumors in infancy and childhood

## FAULKNER HOSPITAL

- Staff—2 Operative and dry clinic  
 E. G. BRACKETT—2 His operation  
 H. C. MARBLE—2 15 Winger hands  
 GORDON M. MORRISON—3 30 Bony block in arthritic knees corrected by operation, motion pictures  
 OTTO J. HERMANN—2 55 Os calcis fractures, motion pictures  
 DR. NEWTON—3 10 Thoracic surgery  
 JOHN ADAMS—3 25 Hip cases, drilling and pinning  
 H. L. JOHNSON—3 45 Stimulation of fracture repair by embryological regime  
 JOHN HOMANS, C. G. MIXER, R. H. SMITHWICK, DR. WHITE, E. E. O'NEIL, H. C. MARBLE, and J. S. HODGSON—4 Symposium. Causalgia

## COLLIS P. HUNTINGTON MEMORIAL HOSPITAL

- Staff—2 15 Dry clinic  
 GRANTLEY W. TAYLOR. Choice of treatment in cancer of the oral cavity  
 DAVID WEISBERGER. Changes in the oral mucous membrane due to vitamin deficiency  
 SHIELDS WARREN. Treatment of leukemia by radioactive substances  
 IRA T. NATHANSON. Relation of the hormones to malignant diseases

## MASSACHUSETTS GENERAL HOSPITAL

- A. W. ALLEN and associates—8 Symposium. Duodenal ulcer  
 C. M. JONES and associates—8 Medical considerations  
 A. O. HAMPTON and associates—8 30 Roentgenological diagnosis  
 E. B. BENEDICT—8 50 Gastroscopy, gastritis  
 A. W. ALLEN—9 10 Surgical considerations  
 HOWARD ULFELDER—9 40 Acute perforation  
 C. E. WELCH—10 10 Malfunction of anastomotic stomas and after-care  
 Staff—10 30 Operative clinic  
 V. H. KAZANJIAN—8 Operative and dry clinic. Plastic surgery, presentation of cases operated upon for various deformities  
 L. S. MCKITTRICK and associates—2 Operative and dry clinic. Acute small bowel obstruction  
 RICHARD WARREN—2 Physiological aspects of non-strangulation obstruction, cause of death  
 L. S. MCKITTRICK—2 30 Factors influencing mortality rate  
 S. P. SARRIS—2 40 Diagnosis  
 RICHARD WARREN—3 10 Non operative treatment, practical consideration in the use of the Miller Abbott tube  
 L. S. MCKITTRICK—3 30 Résumé, outline of treatment, results  
 Staff—3 45 Discussion  
 Staff—4 Operations

## MASSACHUSETTS MEMORIAL HOSPITALS

- HOWARD M. CLUTE, CLIFFORD D. HARVEY, CHARLES SZIKLAS, FRANK E. BARTON, and HOLLIS L. ALBRIGHT—8 Operative clinic. Thyroid, gall bladder, stomach and colon  
 ELEANOR FERGUSON, REGINALD HUNT, and M. JEAN BLACK. Demonstrations. Anesthesia  
 Staff—10 Symposium. Sulfonamides  
 CHESTER S. KEEFER. Use of sulfonamides in bacteremia  
 HOWARD M. CLUTE. Use of sulfonamides in peritoneal cavity  
 HOLLIS L. ALBRIGHT. Massive infection of abdominal wall and of the extremities. demonstration of cases  
 SAMUEL N. VOSE. Use of sulfonamides in genito urinary surgery  
 LEIGHTON F. JOHNSON. Use of sulfonamides in nose and throat infections  
 ARTHUR L. HANRAHAN—10 Operative and dry clinic. Treatment of varicose veins and ulcers

## NEW ENGLAND BAPTIST HOSPITAL

- F. H. LAHEY, R. B. CATTELL, S. F. MARSHALL, and R. P. COLCOCK—9 Operative clinic. Thyroid, stomach, colon, and biliary tract  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—9 Anesthesia demonstrations. Regional, spinal, continuous spinal, and general  
 H. D. ADAMS and N. W. SWINTON—1 30 Operative clinic. Thyroid, stomach, colon, rectum, and biliary tract

U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1:30. Demonstrations: Anesthesia.

#### NEW ENGLAND DEACONESS HOSPITAL

F. H. LAHEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCOCK—9. Operative clinic: Thyroid, stomach, colon, and biliary tract.

U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—9. Anesthesia demonstrations: Regional, spinal, continuous spinal, and general.

H. D. ADAMS and N. W. SWINTON—1:30. Operative clinic: Thyroid, stomach, colon, rectum, and biliary tract.

U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1:30. Demonstrations: Anesthesia.

F. H. LAHEY, SARA M. JORDAN, and S. F. MARSHALL—2. Dry clinic: Technique of subtotal and total gastrectomy; medical and surgical management of duodenal and gastric ulcer; treatment of gastrojejunal colic fistula.

HERBERT ADAMS. Diagnosis and treatment of regional ileitis.

#### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

Staff—10. Out-patient clinics: Gynecological, medical, and pediatric.

G. LINDH MULLER—10. Pathological demonstration: Ovarian tumors.

ELSIE BROWN and ILIA GALLEANI—2. Dry clinic: Metabolism.

#### NEW ENGLAND MEDICAL CENTER

(Boston Floating Hospital)

Staff—2. Dry clinic:

REEVE H. BETTS and ALFRED WELLER—2. Pulmonary suppuration, treatment of empyema in children.

RICHARD WAGNER and W. S. LEVENSON—2:30. Endocrinology and surgery.

FRANCIS McDONALD and R. G. FREEMAN—3. Appraisal of the host, nutrition, personality.

FRANCIS McDONALD, W. S. LEVENSON, NICHOLAS WERTHESEN, and H. E. MACMAHON—3:30. Case of adrenal dysfunction.

H. E. CHAMBERLIN—4. Genito-urinary surgery in children.

W. A. MACCOLL—4:30. Tonsils and adenoids, indications for removal.

#### PALMER MEMORIAL HOSPITAL

Staff—9. Symposium: Carcinoma of the rectum and anus. L. S. MCKITTRICK. Choice of operation in cases of carcinoma of the rectum.

W. F. LEADBETTER. Urological complications after excision of the rectum.

C. C. FRANSENF. Use of electrocoagulation and radium implantation in poor-risk cases of rectal carcinoma.

J. H. MARKS. X-ray therapy of carcinoma of the rectum.

R. H. SWIFT. End-results of treatment of carcinoma of the rectum and anal canal.

#### ST. ELIZABETH'S HOSPITAL

Staff—9. Operative and dry clinic:

JOSEPH STANTON—9. Cholecystectomy.

JOHN SPELLMAN—9. Resection of large bowel.

JOSEPH STANTON—10. Hysterectomy.

FRANCIS JANTZEN—10. Herniorrhaphy.

WILLIAM SANTORO—11. Cholecystectomy.

MARTIN H. SPELLMAN—11. Herniorrhaphy.

ROGER T. DOYLE—11. Presentation of cases.

JOHN F. CASEY—11:45. The use of sulfonamides in general surgery.

#### UNITED STATES NAVAL HOSPITAL

JOSEPH B. LOGUE—9. Operations.

LAWRENCE J. MCCARTHY and FRANKLIN G. BALCH, JR.—9. Operative and dry clinic: Gastro-intestinal diseases, partial gastrectomy for pyloric obstruction; synopsis of case histories.

#### Friday

#### BETH ISRAEL HOSPITAL

Staff—9. Dry clinic:

C. G. MIXTER. Results of surgery of colon neoplasms classified according to extent of lesion.

L. E. BARRON. Pitfalls in diagnosis of carcinoma of stomach, observations in 300 cases.

C. G. MIXTER. Results of surgery of gastric neoplasms classified according to extent of lesion.

I. T. NATHANSON. Surgical management of lymph nodes in cancer surgery.

KARL PRESSER. Differential diagnosis of gastric ulcer by radiography.

JACOB FINE—10:30. Operation: Colon resection.

C. G. MIXTER—10:30. Operation: Gastric resection.

Staff—2. Dry clinic:

A. M. SELIGMAN. Vitamin K<sub>1</sub> in treatment of hypoprothrombinemia in infants.

J. J. MICHAELS and ETHEL COHEN. Psychiatric considerations in surgical patients.

B. E. F. RISEMAN. The surgical treatment of angina pectoris.

S. A. ROBINS. Diagnosis of non-calcified dermoid cysts.

A. M. SELIGMAN. Carcinogenic agents.

H. L. CABITT. Surgical management of pulmonary tuberculosis.

AARON THURMAN. Thoracic esophageal diverticulum.

NAAMAN STEINBERG. Injection treatment of hemorrhoids.

#### BOSTON CITY HOSPITAL

Staff—2. Dry clinic:

C. G. SHEDD—2. Chemotherapy in general peritonitis.

MAXWELL FINLAND—2:30. Chemotherapy in surgery.

R. H. ALDRICH—3:15. The dymical treatment of burns with especial reference to shock.

H. G. DUNPHY—4:15. "Z" plastics in burns.

#### PETER BENT BRIGHAM HOSPITAL

ELLIOTT C. CUTLER and ROBERT ZOLLINGER—9. Operations: Cholecystectomy, choledochostomy.

ELLIOTT C. CUTLER and associates—10. Symposium: Surgical diseases of the biliary tract.

ELLIOTT C. CUTLER. Biliary calculus, technique of surgical therapy.

MERRILL C. SOSMAN. Upright films of the gall bladder as an aid in the diagnosis of cholelithiasis.

ROBERT ZOLLINGER. Acute cholecystitis.

THOMAS B. QUIGLEY. Surgery of the biliary tract in the aged.

WILLIAM A. DAVIS. Clinical use of vitamin K in surgery of the biliary tract.

EDWARD S. EMERY, JR. Medical treatment after cholecystectomy.

ELLIOTT C. CUTLER and associates—2. Symposium: Surgical treatment of hyperthyroidism.

ELLIOTT C. CUTLER. The domain of thyroid surgery.

SAMUEL A. LEVINE. Pre-operative and postoperative treatment of severe thyrocardiacs.

MARSHALL N. FULTON. Recurrent hyperthyroidism.

J. ENGBERT DUNPHY. Use of silk in surgery of the thyroid.

- HARRY B. FRIEDGOOD Role of the pituitary hormone in thyrotoxicosis  
 ELLIOTT C. CUTLER Technique of thyroidectomy

### CARNLY HOSPITAL

- A. MCK. FRASER, WILLIAM E. BROWNE, and staff—9  
 Operative clinic Gastro intestinal, biliary tract, thyroid, and hand

### CHILDREN'S HOSPITAL

- WILLIAM L. LADD and associates—9 Operations

### MASSACHUSETTS GENERAL HOSPITAL

- E. D. CHURCHILL, OLIVER COPE and associates—9 Symposium Hyperparathyroidism  
 J. C. AUB—9 Physiology of the parathyroid glands  
 FULLER ALBRIGHT—9 20 Clinical aspects of hyperparathyroidism  
 TRACY B. MALLORY—9 50 Pathology of the parathyroid glands  
 OLIVER COPE—10 Surgical treatment of hyperparathyroidism  
 F. A. SIMONE—10 35 Renal complications of hyperparathyroidism  
 Staff—11 Operative clinic  
 Staff—2 Symposium Peripheral vascular disease, acute venous thrombosis in veins of lower extremities, pulmonary embolism  
 RICHARD WARREN—2 Fundamental considerations of thrombus formation, clinical manifestations, diagnosis and treatment  
 H. H. FAXON—3 20 Pulmonary embolism, its relation to venous thrombosis  
 RICHARD WARREN—2 45 The use of heparin in the prevention of pulmonary emboli  
 C. E. WELCH and C. E. MCGAHEY—3 Venography, indications, technique, results  
 H. H. FAXON—3 15 Exploration and division of the femoral vein, indications and operative technique  
 C. E. WELCH—3 35 Results, early and late, after division of the femoral vein  
 Staff—3 50 Discussion  
 H. H. FAXON, C. E. WELCH, and RICHARD WARREN—4 Operative clinic

### MASSACHUSETTS MEMORIAL HOSPITALS

- HOWARD M. CLUTE, CLIFFORD D. HARVEY, CHARLES SEIKLAS, FRANK E. BARTON, and HOLLIS L. ALBRIGHT—8 Operative clinic Thyroid, gall bladder, stomach, and colon.  
 ELEANOR FERGUSON, REGINALD HUNT, and M. JEAN BLACK Demonstrations Anesthesia  
 REGINALD HUNT—10 30 Dry clinic Spinal headaches, preliminary report

- M. JEAN BLACK Relative efficiency of different methods of oxygen therapy

### NEW ENGLAND BAPTIST HOSPITAL

- F. H. LAHEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCOCK—9 Operative clinic Thyroid, stomach, colon, and biliary tract  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—9 Anesthesia demonstrations Regional, spinal, continuous spinal, and general  
 H. D. ADAMS and N. W. SWINTON—1 30 Operative clinic Thyroid, stomach, colon, rectum, and biliary tract  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1 30 Demonstrations Anesthesia

### NEW ENGLAND DEACONESS HOSPITAL

- F. H. LAHEY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCOCK—9 Operative clinic Thyroid, stomach, colon, and biliary tract  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—9 Anesthesia demonstration Regional, spinal, continuous spinal and general  
 H. D. ADAMS and N. W. SWINTON—1 30 Operative clinic Thyroid, stomach, colon, rectum, biliary tract  
 U. H. EVERSOLE, LEO V. HAND, and M. J. NICHOLSON—1 30 Demonstration Anesthesia

### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

- Staff—10 Out patient clinics Gynecological, ophthalmological, vascular, and pediatric (cardiac)

### PALMER MEMORIAL HOSPITAL

- Staff—2 Symposium Diabetic gangrene  
 H. F. ROOT Medical aspects  
 L. S. MCKITTRICK Principles of surgical treatment, classification of lesions, conservative methods  
 T. C. PRATT Indications for and technique of minor amputation  
 L. S. MCKITTRICK Indications for and technique of major amputation  
 T. C. PRATT End result study of 100 patients after supracondylar amputation for gangrene  
 L. S. MCKITTRICK and T. C. PRATT—2 Operations Supracondylar amputations for gangrene

### ST ELIZABETH'S HOSPITAL

- JOSEPH STANTON and staff—9 Operations

### SALEM HOSPITAL

- Staff—10 Clinicopathological conference

### UNITED STATES NAVAL HOSPITAL

- CHARLES H. SWAN—9 Operations

# OBSTETRICS AND GYNECOLOGY

## Tuesday

### BOSTON CITY HOSPITAL

Staff—2. Symposium: Pregnancy, the physiological and pathological aspects.

GEORGE R. MINOT and EUGENE L. LOZNER—2. The hemorrhagic diatheses complicating pregnancy.

FREDERICK J. LYNCH—2:30. Treatment of miscarriage.

FREDERICK PARKER, JR.—3. Pathology of toxemia of pregnancy with special reference to changes in the placenta.

CARM R. ALDEN—3:30. Disorders of the urinary tract, encountered in obstetrics.

BENEDICT F. BOLAND—4. Hormonal relationship between the kidneys and toxemia of pregnancy.

MAXWELL FINLAND—4:20. Pneumonia in pregnancy.

### BOSTON LYING-IN HOSPITAL

Staff—10. Operative and dry clinic:

CHARLES A. JANEWAY. Treatment of puerperal sepsis with sulfanilamide and immune transfusions.

CLEMENT A. SMITH. Quantitative measurements of anesthesia and anoxia produced in mother and infant by obstetrical anesthetics.

### CARNEY HOSPITAL

LOUIS E. PHANEUF and staff—9. Operative clinic.

Staff—2. Dry clinic:

LOUIS E. PHANEUF. Manchester operation in management of uterine prolapse.

R. J. HEFFERNAN. Conservative management of premature separation of the placenta.

ROGER C. GRAVES and LOUIS E. PHANEUF. Management of difficult vesicovaginal fistula.

H. EDWARD MACMAHON. Biopsy of uterine cervix from the standpoint of the pathologist.

MAURICE O. BELSON. Uterine hemorrhage; technique of uterovaginal tamponade.

EDMUND L. CAREY. Analysis of breech deliveries at the Carney Hospital during the last 10 years.

WILLIAM C. MALONEY. Abnormal capillary fragility in the newborn.

### FREE HOSPITAL FOR WOMEN

JOHN ROCK and SIDNEY C. GRAVES—3. Operations.

Staff—9. Symposium: Carcinoma of the cervix.

FRANK A. PEMBERTON—9. Radium application. Demonstration of radium applicators.

FRANK A. PEMBERTON and RICHARD DRESSER—9:20. Present methods of radium and x-ray treatment.

ARTHUR T. HERTIG and PAUL A. YOUNGE—9:40. Diagnosis of early carcinoma, clinical and pathological.

GEORGE VAN S. SMITH—10:40. Complications and treatment.

PAUL A. YOUNGE—11. Urological complications.

GEORGE VAN S. SMITH—11:20. Results and summary.

PAUL A. YOUNGE—11:45. Hysterectomy for early carcinoma of the cervix.

### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

LETTIA DOUGLAS ADAMS, BLANCHE L. ATWOOD, ILIA GALLEANI, and GRACE E. ROCHFORD—9. Operations.

MARJORIE WOODMAN—2. Obstetrical analgesia.

ESTHER E. BARTLETT—2. Demonstration: Pudendal and parasacral blocks in obstetrical anesthesia.

### PALMER MEMORIAL HOSPITAL

G. A. LELAND, JR. and C. J. SWAN—2. Symposium: Treatment of carcinoma of the cervix.

### ST. ELIZABETH'S HOSPITAL

Staff—9. Demonstration: Technique of normal delivery.

FREDERICK L. GOOD and staff—10. Operations.

## Wednesday

### BOSTON CITY HOSPITAL

Staff—9. Dry clinic: Anesthesia and analgesia with special reference to spinal and intravenous anesthesia.

DR. REGINALD and R. D. MARGESON—9:30. Placenta previa in patients previously delivered by low transverse cesarean section.

FREDERICK L. GOOD—10. Physiology of the lower uterine segment.

D. J. MCSWEENEY—10:30. Radiographic pelvimetry.

F. W. O'BRIEN—11. Results in treatment of carcinoma of the uterus in the tumor clinic of a general hospital.

FREDERICK PARKER, JR., and JOHN T. WILLIAMS—11:30. Pathology of so-called fibrosis of the uterus.

### BOSTON LYING-IN HOSPITAL

Staff—2. Dry clinic:

MEINOLPH V. KAPPIUS. The rôle of soft tissue x-ray technique in the diagnosis of placenta previa.

ROBERT N. RUTHERFORD. Interpretation of bleeding in the first trimester of pregnancy as shown by endometrial biopsies.

ARTHUR T. HERTIG. Pathological ova, chief cause of spontaneous abortion.

ROBERT H. BARKER. Determination of cephalopelvic disproportion by Thoms method of roentgenometry.

### CARNEY HOSPITAL

LOUIS E. PHANEUF and staff—9. Operative clinic.

### FREE HOSPITAL FOR WOMEN

EDWARD B. SHEEHAN and CHRISTOPHER J. DUNCAN—8. Gynecological operations.

Staff—9. Dry clinic: Carcinoma of the endometrium.

FRANK A. PEMBERTON—9. Hysterectomy for carcinoma of the endometrium.

FRANK A. PEMBERTON and RICHARD DRESSER—10. Methods of treatment, surgery, radium and x-ray.

ARTHUR T. HERTIG—10:30. Pathology and diagnosis of early carcinoma.

GEORGE VAN S. SMITH—11. Results and summary.

PAUL A. YOUNGE—11:30. Biopsy and cauterization of the cervix in ambulatory patients.

### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

Staff—9. Operations.

MARJORIE WOODMAN—9:30. Obstetrical ward rounds.

MARJORIE WOODMAN—2. Obstetrical analgesia.

ESTHER E. BARTLETT—2. Demonstration: Parasacral and pudendal blocks in obstetrical anesthesia.

### PONDVILLE HOSPITAL

JOE V. MEIGS, LANGDON PARSONS, and associates—9. Operative clinic: Wertheim operation for cancer of the cervix; dissection of pelvic lymph nodes (Tauszig operation); radium treatment for cancer of the cervix.

# SURGERY, GYNECOLOGY AND OBSTETRICS

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## ST. ELIZABETH'S HOSPITAL

CHARLES J. KICKHAM—9 Low transverse cervical section, plastic and laparotomy for prolapse of uterus  
FREDERICK L. GOOD and staff—10 Operations

Thursday

## BOSTON LYING-IN HOSPITAL

Staff—10 Operative and dry clinic.  
JOHN L. NEWELL External cephalic version as prophylaxis against the fetal hazards of breech presentations  
DANIEL ABRAMSON End results of a conservative policy at delivery as shown in a study of postpartum patients

## CARNEY HOSPITAL

LOUIS F. PHANEUF and staff—9 Operative clinic  
FREE HOSPITAL FOR WOMEN

SIDNEY C. GRAVES and PAUL A. YOUNG—8 Gynecological operations  
Staff—9 Symposium Fertility and hormones in gynecology

JOHN ROCK—9 Technique, interpretation and value of endometrial biopsy  
JOHN O. HAMAN—9 30 Time relationship of ovulation to menstruation  
FRED A. SIMMONS—10 Evaluation and improvement of the male in a sterile mating  
JOHN ROCK—10 30 Clinical lessons from seven pre-villous embryos  
GEORGE VAN S. SMITH—11 Hormones in gynecology  
W. STEWART WHITTEMORE (from the Cambridge Hospital)—11 30 A case of artificial vagina, pregnancy and cesarean section

Staff—2 Dry clinic  
PAUL A. YOUNG—2 Results of presacral neurectomy for pelvic pain  
ROBERT TUCKER—2 30 A follow up study of cases found to have cholelithiasis at the time of lower abdominal surgery  
PAUL A. YOUNG—3 The treatment of interstitial cystitis  
FRANK A. PEMBERTON—3 30 The treatment of endometriosis

## MASSACHUSETTS MEMORIAL HOSPITALS

C. WESLEY SEWALL, JOHN J. ELLIOTT, and JOHN C. V. FISHER—8 Operative clinic Low cervical cesarean, low forceps, mid forceps, ward walk with demonstration of nursery  
C. WESLEY SEWALL and staff—2 Dry clinic  
JOHN J. ELLIOTT A ten year study at the Massachusetts Memorial Hospitals of bleeding in the third trimester of pregnancy  
OWEN C. MULLANEY Prenatal and postnatal care  
JOHN C. V. FISHER A ten year survey of cesarean section at the Massachusetts Memorial Hospitals  
MAX DAVIS The physiology and clinical application of testosterone  
KENNETH W. SEWALL A twenty year survey of eclampsia at the Massachusetts Memorial Hospitals  
HERMAN C. PETERSON Modern care of the newborn

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

MARJORIE WOODMAN—9 30 Operation Cesarean Previous operation on bicornate uterus  
MARJORIE WOODMAN—2 Obstetrical analgesia

ESTHER L. BARTLETT—2 Demonstration Pudendal and pirasacral blocks in obstetrical anesthesia

## ST. ELIZABETH'S HOSPITAL

Staff—10 Dry clinic and ward visits Technique of care of breasts in puerperium, review of cesarean sections for the past 10 years  
CHARLES J. KICKHAM—11 Plastic operation for lacerated cervix and perineum

Friday

## CARNEY HOSPITAL

LOUIS E. PHANEUF and staff—9 Operative clinic  
FREE HOSPITAL FOR WOMEN

GEORGE VAN S. SMITH and MEINOLF V. KAPPLIS—8 Gynecological operations  
Staff—9 Operative and dry clinic Tumors of the ovary  
GEORGE VAN S. SMITH—9 Ovarian tumor  
ARTHUR T. HERTIG—10 X ray treatment  
RICHARD DRESSER—10 30 Results in the treatment of carcinoma of the ovary  
FRANK A. PEMBERTON—11 Pruritus, kraurosis, leukoplakia and carcinoma of the vulva, etiology, treatment and results

## MASSACHUSETTS GENERAL HOSPITAL

JOE V. MEIGS and associates—9 Operative and dry clinic  
JOE V. MEIGS, LANGDON PARSONS and MARSHALL F. BARTLETT—9 Total abdominal hysterectomy for prolapse, Bassett's operation for cancer of the vulva modified Kennedy operation for repair of urethral continence  
SOMERS STURGIS Dysmenorrhea, treatment with estrogens  
WARD I. GREGG Metropathia hemorrhagica, treatment with prolon  
IRA T. NATHANSON Treatment for painful breasts with testosterone  
LANGDON PARSONS Carcinoma of the vulva  
MARSHALL F. BARTLETT Treatment for incontinence  
JOE V. MEIGS Fibroma of the ovary with fluid in the abdomen and chest

## NEW ENGLAND DLACONESS HOSPITAL

FRANK FOSTER—1 30 Dry clinic Sterility problem, menstrual abnormalities  
B. P. COCKOCK—1 30 Dry clinic Endometriosis, severe primary dysmenorrhea

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

Staff—9 Operations  
Staff—9 30 Dry clinic Prenatal and postpartum care

## ST. ELIZABETH'S HOSPITAL

FREDERICK L. GOOD and staff—9 Operations

## UNITED STATES NIVAL HOSPITAL

JOSEPH B. DOYLE—10 Colored motion pictures of spinal anesthesia in obstetrics, discussion of case histories

Days to be Announced

EVANGELINE BOOTH MATERNITY HOSPITAL  
A. K. PANF, W. J. McDONALD, H. S. FINKE, M. G. BEKLY, J. E. HOPKINS, D. C. GOLDFARB, A. A. LEVI, L. ALBERT, S. ELLIS, J. TARTAKOFF, and S. SIDELL  
Operative and Dry Clinics

# THORACIC SURGERY

## Monday

MASSACHUSETTS MEMORIAL HOSPITALS  
JOHN W. STRIEDER and W. W. WOODRUFF (Saranac Lake, New York)—2. Symposium: Thoracic surgery. Suppurative pericarditis, colored moving pictures; lobectomy for bronchiectasis; tuberculous empyema.

NEW ENGLAND BAPTIST HOSPITAL  
H. D. ADAMS—1:30. Operations.

NEW ENGLAND DEACONESS HOSPITAL  
RICHARD H. OVERHOLT and REEVE H. BETTS.—2. Operative clinic: Non-tuberculous thoracic surgery.

## Tuesday

NEW ENGLAND BAPTIST HOSPITAL  
H. D. ADAMS—1:30. Operations.

NEW ENGLAND DEACONESS HOSPITAL  
Staff—2. Dry clinic: Symposium on total pneumonectomy.

REEVE H. BETTS. Determination of operability in primary carcinoma of the lung.  
SHIELDS WARREN. Pathology of lung cancer.  
RICHARD H. OVERHOLT. Exploratory thoracotomy in suspected malignancy.  
BERT H. COTTON. Use of sulfathiazole in pulmonary resection.

ANDREW YEOMANS. Physiological observations made at time of pulmonary resection.  
PHILLIP SCHULTZ. Problems of anesthesia in pneumonectomy.

HOWARD ROOT. Medical aspects of postoperative management.  
Staff. Presentation of cases treated by pneumonectomy for cancer, tuberculosis, bronchiectasis, and cystic disease.

## Wednesday

COREY HILL HOSPITAL  
Staff—2. Operative clinic: Pulmonary tuberculosis.

MASSACHUSETTS GENERAL HOSPITAL  
E. D. CHURCHILL and associates—9. Symposium and clinic: Primary tumors of the lung and esophagus.  
D. S. KING—9. Medical aspects of primary carcinoma of the lung.

E. D. CHURCHILL—9:20. Types of operations and results in carcinoma of the lung.  
R. H. SWEET—9:30. Resection of the lung for metastatic sarcoma.

R. H. SWEET—10. Surgical treatment of carcinoma of the lower third of the esophagus and cardiac area of the stomach.

E. D. CHURCHILL—10:30. Surgical treatment of carcinoma of the upper two-thirds of the esophagus.  
ROBERT KLOPSTOCK—10:45. Discussion and exhibition of gross pathological specimens.  
Staff—11. Operations.

MASSACHUSETTS MEMORIAL HOSPITALS  
JOHN W. STRIEDER—2. Operative clinic: Lobectomy for bronchiectasis; thoracoplasty for tuberculosis.

NEW ENGLAND BAPTIST HOSPITAL  
H. D. ADAMS—1:30. Operations.

NEW ENGLAND DEACONESS HOSPITAL  
H. D. ADAMS—1:30. Operations.

## Thursday

MASSACHUSETTS GENERAL HOSPITAL  
E. D. CHURCHILL and associates—2. Operative and dry clinic: Suppurative lesions of the lung.  
D. S. KING—2. Medical aspects of bronchiectasis, prognosis of untreated cases.  
L. DAVENPORT—2:20. Technique of bronchography and anatomy of bronchial tree.  
E. D. CHURCHILL—2:40. The surgical treatment of bronchiectasis.  
R. H. SWEET—3. Surgical treatment of lung abscess, results.  
E. D. CHURCHILL—3:30. Lobectomy and pneumonectomy in lung abscess.  
ROBERT KLOPSTOCK—3:45. Discussion and exhibition of gross pathological specimens.

NEW ENGLAND BAPTIST HOSPITAL  
H. D. ADAMS—1:30. Operations.

## Friday

BOSTON CITY HOSPITAL  
Staff—9. Operative and dry clinic:  
J. W. STRIEDER—9. Colored motion pictures of suppurative pericarditis; result of modern method of treatment of putrid empyema; lobectomy for bronchiectasis.  
HORACE BINNEY—9:45. Methods and results of treatment of pulmonary tuberculosis.  
S. J. G. NOWAK—10:45. Experimental pulmonary embolus.  
DR. SHULTZ—11:30. Intratracheal anesthesia for thoracic surgery.

NEW ENGLAND DEACONESS HOSPITAL  
Staff—2. Symposium on total pneumonectomy.  
REEVE H. BETTS. Determination of operability in primary carcinoma of the lung.  
SHIELDS WARREN. Pathology of lung cancer.  
RICHARD H. OVERHOLT. Exploratory thoracotomy in suspected malignancy.  
BERT H. COTTON. Use of sulfathiazole in pulmonary resection.  
ANDREW YEOMANS. Physiological observations made at time of pulmonary resection.  
PHILLIP SCHULTZ. Problems of anesthesia in pneumonectomy.  
HOWARD ROOT. Medical aspects of postoperative management.  
Staff. Presentation of cases treated by pneumonectomy for cancer, tuberculosis, bronchiectasis, and cystic disease.

NEW ENGLAND BAPTIST HOSPITAL  
H. D. ADAMS—1:30. Operations.

## ORTHOPEDIC SURGERY

## Tuesday

## CHILDREN'S HOSPITAL

FRANK R. OBER and associates—9 Operations

## NEW ENGLAND BAPTIST HOSPITAL

G. E. HAGGART and J. W. TOUMAY, JR.—9 Operations

## NEW ENGLAND DEACONESS HOSPITAL

G. F. HAGGART and J. W. TOUMAY, JR.—9 Operations

## Wednesday

## ROBERT BRECK BRIGHAM HOSPITAL

Staff—9 Operative Clinic

JOHN G. KUHN'S Arthroplasty of elbow.

ROBERT J. JOPLIN Posterior capsularplasty of knee for flexion deformity

WILLIAM A. ELLISTON Osteotomy for malum coxae senilis

Staff—2 Symposium End results in correction of arthritic deformities

LORING T. SWAIM Treatment of spinal arthritis

JOHN G. KUHN'S Correction of contractures of the knee

ROBERT J. JOPLIN End results in arthroplasties of elbow

JOHN A. REIDY Arthroplasties of knee

WILLIAM A. ELLISTON Treatment of osteo-arthritis of hip

## CARNEY HOSPITAL

W. R. MACLESLAND and staff—9 Operative clinic.

## CHILDREN'S HOSPITAL

Staff—9 Dry clinic

WILLIAM A. ELLISTON Study in bone growth and resorption of the epiphyseal plate

LEO J. McDERMOTT Equalization of leg length, leg lengthening

PAUL W. HUGENBERGER Tuberculosis of bone

ALBERT H. BREWSTER Arthrodesis of the foot in spastic paralysis

Staff—11 Symposium Infantile paralysis, operative treatment, round table discussion.

## MASSACHUSETTS MEMORIAL HOSPITALS

LOUIS G. HOWARD, KENNETH CHRISTOPHE, and WILLIAM A. ELLISTON—9 Operative clinic Spinal fusion, hip reconstruction with vitallium cup

## NEW ENGLAND BAPTIST HOSPITAL

G. E. HAGGART and J. W. TOUMAY, JR.—9 Operations

## NEW ENGLAND DEACONESS HOSPITAL

G. F. HAGGART and J. W. TOUMAY, JR.—9 Operations

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

MIRIAM G. KATZEFF—9 Operations Dry clinic Arthritis, fractures, x rays of pathological bone conditions clubfoot demonstration

## ST ELIZABETH'S HOSPITAL

THOMAS F. BRODERICK—9 Spinal fusion Dry clinic Motion pictures of author's technique of spinal fusion.

## UNITED STATES NAVAL HOSPITAL

THOMAS H. PETERSON—9 Dry clinic Shoulder injuries, discussion of case histories; x ray findings

## Thursday

## CHILDREN'S HOSPITAL

FRANK R. OBER and associates—9 Operations

## FAULKNER HOSPITAL

F. G. BRACCAET, H. C. MARBLE, G. M. MORRISON, J. L. DOHERTY, J. D. ADAMS, and OTTO J. HERMANN—8 Operative clinic.

HARVEY MORRISON X ray demonstrations

## MASSACHUSETTS GENERAL HOSPITAL

M. N. SMITH PETERSEN and associates—2 Operative and dry clinic

M. N. SMITH-PETERSEN, ARMIN KLEIN, J. S. BARR, and PAUL L. NORTON—2 Operations

WILLIAM A. ROGERS—2 Fractures and fracture dislocations of the cervical spine, results of operative treatment.

GEORGE VAN GORDER Amputations

E. F. CAVE. Fractures of the carpal scaphoid, results of bone graft.

O. SHERWIN STAPLES Effect on the knee joint of pan-astragalar arthrodesis

OTTO E. AUFRANC, CARROLL B. LAWSON, and M. N. SMITH-PETERSEN Surgical procedures for relief of deformities arising from rheumatoid arthritis

WALTER BAUFER Discussion

## MASSACHUSETTS MEMORIAL HOSPITALS

LOUIS G. HOWARD, ALBERT H. FERGUSON, and THOMAS J. ANGLE—9 Discussion of malignant bone tumors

## NEW ENGLAND BAPTIST HOSPITAL

G. E. HAGGART and J. W. TOUMAY, JR.—9 Operations

## NEW ENGLAND DEACONESS HOSPITAL

G. E. HAGGART and J. W. TOUMAY, JR.—9 Operations

## ST ELIZABETH'S HOSPITAL

THOMAS F. BRODERICK and staff—9 Operations

## Friday

## CARNEY HOSPITAL

W. R. MACLESLAND and staff—9 Operative clinic

## CHILDREN'S HOSPITAL

Staff—9 Dry clinic followed by round table discussion

MIRIAM G. KATZEFF—9 Early treatment of clubfoot

ROBERT H. MORRIS—9 20 Treatment of difficult club foot

FRANK R. OBER—9 10 Treatment of congenital elevation of the scapula

WILLIAM T. GREEN—10 10 Osteochondritis dissecans

MEIER G. KARP—10 45 Fractures about the elbow

Staff—11 15 Congenital malformations

## MASSACHUSETTS GENERAL HOSPITAL

M. N. SMITH PETERSEN and associates—8 10 Operative and dry clinic

# PROGRAM FOR THE BOSTON CLINICAL CONGRESS

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J. W. VANGORDER, W. A. ROGERS, and E. F. CAVE—  
8:30. Operations.  
ARMIN KLEIN, JOHN A. REIDY, and ROBERT J. JOPLIN—  
9. Slipped upper femoral epiphysis, results of oper-  
ative and non-operative treatment.  
JOSEPH S. BARR. Spinal fusion, frequency of pseud-  
arthrosis.  
M. N. SMITH-PETERSEN, CARROLL E. LARSON, and OTTO  
E. AUFRANC. Arthroplasty of the hip, results.

NEW ENGLAND BAPTIST HOSPITAL  
G. E. HAGGART and J. W. TOUMEX, JR.—9. Operations.  
NEW ENGLAND DEACONESS HOSPITAL  
G. E. HAGGART and J. W. TOUMEX, JR.—9. Operations.  
UNITED STATES NAVAL HOSPITAL  
THOMAS H. PETERSON—9. Operations.

## GENITO-URINARY SURGERY

Tuesday

### BETH ISRAEL HOSPITAL

Staff—9. Dry clinic:  
E. G. CRABTREE. Pre-operative preparation of prostatic  
cases.  
G. C. PRATHER and M. L. BRODNY. Accessory bladder  
pathology in prostatic cases.  
G. C. PRATHER and MORTIMER REICH. Accessory renal  
pathology in prostatic cases.  
E. G. CRABTREE. Summary of 12 years' experience in  
prostatic surgery.  
G. C. PRATHER. Results of contact therapy for bladder  
tumors.  
E. G. CRABTREE—10:45. Operation: Bladder tumor, con-  
tact radiation therapy.  
Staff—2. Dry clinic:  
E. L. PRIEN. Adaptation of the Tratner hydrophoro-  
graph for bladder studies.  
ABRAHAM ZIMMERMAN. Bladder atonies.  
J. H. LIPTON. Bladder atonies as demonstrated by the  
Tratner hydrophorograph.  
S. R. MUELLNER. Testosterone effect on bladder tone;  
diabetic atony of the bladder.  
B. E. GREENBERG. Value of cholinergic and adrenergic  
drugs in bladder atonies.  
H. A. KONTOFF. Rate of recovery of bladder after re-  
lief of obstruction.  
S. R. MUELLNER. Stress incontinence in the female.  
E. L. PRIEN. Crystallography of the sulfonamide drugs.

### CHILDREN'S HOSPITAL

WILLIAM E. LADD and associates—9. Dry clinic: Diseases  
of the genito-urinary tract in infancy and childhood,  
followed by questions and discussion.  
WILLIAM E. LADD. Embryoma of the kidney (Wilms'  
tumor).  
ROBERT E. GROSS. Surgical treatment of malforma-  
tions.  
THOMAS H. LANMAN. Exstrophy and epispadias.

### MASSACHUSETTS MEMORIAL HOSPITALS

Staff—9. Operative clinic:  
M. J. HAEN—9. Pyelotomy for stone.  
DAVID B. STEARNS—10. Suprapubic prostatectomy.  
SAMUEL N. VOSE—11. Perineal prostatectomy.

### NEW ENGLAND BAPTIST HOSPITAL

E. E. EWERT and VERNON S. DICK—9. Operations.

### NEW ENGLAND DEACONESS HOSPITAL

E. E. EWERT and VERNON S. DICK—9. Operations.

### ST. ELIZABETH'S HOSPITAL

EDWARD J. O'BRIEN and associates—10. Operations.

Wednesday

MASSACHUSETTS GENERAL HOSPITAL  
G. G. SMITH and associates—9. Operative and dry clinic:  
Staff—9. Operations.  
F. H. COLBY—10:30. Genito-urinary tuberculosis.  
RICHARD CHUTE—10:50. Results of treatment with  
estrogenic substances in prostatic hypertrophy.  
S. B. KELLEY—11:10. Complications of transurethral  
resection.  
LORANDE WOODRUFF—11:40. The female urethra.  
G. G. SMITH and associates—2. Operative and dry clinic;  
Staff—2. Operations.  
G. G. SMITH—3:30. Treatment of prostatic cancer.  
ARTHUR WILLETS—3:50. Chronic prostatitis.  
WYLAND LEADBETTER—4:10. Renal arteriography.  
JOHN GENS—4:30. Urological endocrinology.

### MASSACHUSETTS MEMORIAL HOSPITALS

Staff—9. Symposium: Obstructing prostate.  
CLYDE L. DEMING (New Haven, Connecticut). Func-  
tional end-results following perineal prostatectomy.  
EDWARD N. COOK (Rochester, Minnesota). Pre-opera-  
tive preparation for transurethral prostatectomy.  
SAMUEL N. VOSE. Selection of operative procedure.  
JOSEPH F. MCCARTHY (New York). Technical aspects  
of prostatic resection with commentary on pharmaco-  
logical adjuvants.

### NEW ENGLAND BAPTIST HOSPITAL

E. E. EWERT and VERNON S. DICK—9. Operations.

### NEW ENGLAND DEACONESS HOSPITAL

HARVARD H. CRABTREE—9. Operations.  
E. E. EWERT and VERNON S. DICK—9. Operations.

### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

SUSANNAH FRIEDMAN—2. Dry clinic: End-results of  
pyelitis of pregnancy.

### NEWTON HOSPITAL

E. G. CRABTREE, G. C. PRATHER, and E. L. PRIEN—9.  
Operations.  
Staff—2. Dry clinic:  
E. L. PRIEN. Analysis of calcifications and crystals in  
renal tissue.  
G. C. PRATHER. Cystin stone and cysteinuria.  
E. G. CRABTREE. Block dissections for renal tumor and  
cancer of the bladder.  
G. C. PRATHER. Calyceal diverticula.  
E. L. PRIEN. Multiple recurrent stones, palliation.  
E. G. CRABTREE. Uretero-nephrectomy.  
G. C. PRATHER. Graphic evidence of upper urinary dila-  
tation with lower urinary obstruction.



## PONDVILLE HOSPITAL

- ROGER C. GRAVES and associates—9 Operative clinic:  
Carcinoma of the bladder.  
Staff—11 Dry clinic:  
ROGER C. GRAVES. Carcinoma of the bladder.  
CHARLES C. J. KICKHAM Urological complications in  
carcinoma of the rectum and colon  
WESTON T. BUDDINGTON Urological complications in  
carcinoma of the cervix

## Thursday

## BETH ISRAEL HOSPITAL

- Staff—9 Dry clinic  
E. L. PRIEN. A new method for stone analysis  
D. B. STEARNS. Parathyroid disease and urinary lithiasis  
G. C. PRATHER. Roentgenology of kidney at operation.  
B. E. GREENBERG. Use of cholinergic and adrenergic  
medication for ureteral stone passage  
H. A. KONTOFF. Hospital statistics on urinary lithiasis  
J. H. LIPTON. Clearance of infection in stone cases after  
operation  
D. B. STEARNS. Diagnosis of calyceal calcifications  
H. A. KONTOFF. Renal tumor statistics of the hospital  
Demonstration of surgical specimens of renal tumors  
with pyelographic and microscopic data  
E. G. CRABTREE—11 Operation. Excision of renal tumor  
Staff—2 Dry clinic  
M. L. BRODNY. Fractional phylography  
J. H. LIPTON. Sulfonamide drugs in surgical wounds  
and postoperative infections  
B. E. GREENBERG. Methylene blue treatment for tuber-  
culosis of the bladder.  
E. L. PRIEN. Renal injury from sulfathiazole and sulfa-  
pyridine, nature of the lesion  
D. B. STEARNS. Undescended testicle, age groups  
M. L. BRODNY. Urological study of enuresis cases  
DR. FISHERMAN. Denervation of the kidney, end results  
of 200 cases  
B. E. GREENBERG. Organization and function of a  
sterility clinic  
NATHAN CHASE. Hypertensive disease in urology

## BOSTON CITY HOSPITAL

- Staff—9 Operative and dry clinic  
H. H. HOWARD—9 Epidermoid carcinoma of the penis.  
GEORGE C. PRATHER—9 25 Stricture of the urethra  
S. R. MUELLNER—9 50 Newer concepts of urinary ex-  
travasation  
G. D. ATKINSON—10 15 Scrotal plastics after idio-  
pathic gangrene  
W. H. HOLTHAM—10 40 Treatment of gonorrheal ure-  
thritis with sulfathiazole  
J. A. SEIF—11 0. Removal of calculi from lower ureter  
by the vaginal route, report of 2 cases  
F. G. SHEDDEN—11 25 Fracture of the penis, case re-  
port. Anatomical study of remnants of prostate tissue  
in the prostatic bed following enucleation  
AUGUSTUS RILEY—11 40 Hemangioma of kidney

## PETER BENT BRIGHAM HOSPITAL

- WILLIAM C. QUINBY and associates—2 Symposium  
J. HARTWELL HARRISON. The diagnosis and treatment  
of common injuries of the urinary tract

- GEORGE AUSTEN. A correlation of the clinical aspects  
and pathology of the fused renal mass.  
G. PHILIP GRABFIELD. Renal blood flow.  
F. ANTHONY SIMEONE. Experimental hypertension  
WILLIAM C. QUINBY. A critical evaluation of prostatic  
surgery in recent years

## CARNEY HOSPITAL

- ROGER C. GRAVES and staff—9 Operative clinic

## MASSACHUSETTS GENERAL HOSPITAL

- G. G. SMITH and associates—9 Operative and dry clinic.  
Staff—9 Operations  
HOWARD SUBY—10 30 Solution of urinary calculi  
RICHARD CRUTE—10 50 Problems in the treatment of  
urinary calculi  
F. H. COLEY—11 15 Deep x ray therapy in cancer of  
the bladder  
S. B. KELLEY—11 40 Ureterostomy versus nephros-  
tomy.

## NEW ENGLAND BAPTIST HOSPITAL

- E. E. EWERT and VERNON S. DICK—9 Operations

## NEW ENGLAND DEACONESS HOSPITAL

- E. E. EWERT and VERNON S. DICK—9 Operations

## UNITED STATES NAVAL HOSPITAL

- NICHOLAS G. SCARCELLO—9 Dry clinic. Presentation of  
urological cases with histories and x ray findings

## Friday

## MASSACHUSETTS GENERAL HOSPITAL

- R. H. SMITHWICK and associates—2 Symposium. Sur-  
gery of non nephritic hypertension  
ROBERT S. PALMER. Statement of the problem  
BENJAMIN CASTLEMAN. Renal pathology  
JOHN S. TALBOT. Renal physiology  
RICHARD CRUTE. Urological factors  
R. H. SMITHWICK. Modification of abnormal physiology  
by sympathectomy

## MASSACHUSETTS MEMORIAL HOSPITALS

- Staff—9 Dry clinic  
DAVID B. STEARNS. Prostatovesiculitis simulating upper  
urinary tract symptomatology  
SAMUEL N. VOSE. Radical prostatectomy for cancer of  
prostate  
FRANK MORSE, JR. Congenital bladder neck obstruc-  
tion in male children  
M. F. HAHN, JR. Review of urinary calculus cases at  
the Massachusetts Memorial Hospitals during past  
15 years

## NEW ENGLAND BAPTIST HOSPITAL

- E. E. EWERT and VERNON S. DICK—9 Operations

## NEW ENGLAND DEACONESS HOSPITAL

- E. E. EWERT and VERNON S. DICK—9 Operations

NEW ENGLAND HOSPITAL FOR WOMEN  
AND CHILDREN

- G. LINDH MULLER—10 Pathological demonstration  
Congenital abnormalities of the kidney, nephrolithiasis

## FRACTURES AND OTHER TRAUMAS

*Tuesday*

## BOSTON CITY HOSPITAL

OTTO J. HERMANN and associates—9. Symposium: Fractures of the ankle.

OTTO J. HERMANN. Introduction.

GORDON M. MORRISON. Simple unilateral ankle injuries with fracture.

JOSEPH BURNETT, G. G. BAILEY, JOSEPH SHORTELL, and RUSSELL SULLIVAN. Complicated ankle fractures, bilateral, following Cotton's therapeutical ankle classifications. Slides, charts, individual cases, and apparatus illustrating various points.

*Thursday*

## BEVERLY HOSPITAL

Staff—9. Operative and dry clinic:

PEER P. JOHNSON. Interesting fractures, end-results.

JOHN D. ADAMS. Injuries to hip joint; drilling of femoral neck in dislocation of hip joint.

RICHARD E. ALT. Open reduction in fractures and dislocations.

PAUL E. TIVNAN and JOSEPH A. CUNNINGHAM. Clinico-pathological conference on bone tumors.

JACOB H. FINE. Demonstration of recently constructed operating amphitheater eliminating fire and explosion hazards.

*Friday*

## BOSTON CITY HOSPITAL

Staff—9. Symposium: Fractures of the hip.

NEWTON C. BROWDER—9. Intracapsular fractures of the hip.

RUSSELL SULLIVAN—9:30. Hip fractures, cases of operative reduction and internal fixation.

OTTO J. HERMANN—10. Painful ununited hip fractures.

THOMAS H. PETERSON—10:30. Posterior fusion of the hip.

A. A. THIBODEAU—11. Slipped femoral epiphysis.

JAMES W. SEVER—11:30. Presentation of cases.

DR. WISE (of New York)—11:45. Presentation of autopsy specimens of nailed fractured hips.

## MASSACHUSETTS GENERAL HOSPITAL

A. W. REGGIO, A. W. ALLEN, M. N. SMITH-PETERSEN, H. C. MARBLE, G. W. VANGORDER, and associates—2. Dry clinic.

Staff—2. Fracture rounds; presentation of current cases with open discussion.

Staff—3:30. End-result clinic; presentation of follow-up cases with open discussion of problems.

## UNITED STATES MARINE HOSPITAL

RICHEY L. WAUGH and associates—8. Operative clinic: Internal derangement of knee-joint; bunion, closed treatment, double-pin method; fracture both bones of leg, open treatment using vitallium plate.

RICHEY L. WAUGH and associates—1. Dry clinic:

RICHEY L. WAUGH. Skeletal traction and countertraction methods applicable to ordinary extension splints in the treatment of fractures of lower extremity.

THOMAS A. HATHCOCK. Use of vitallium in fractures.

RICHEY L. WAUGH. Injuries of the wrist.

## NEUROSURGERY

*Monday*

## MASSACHUSETTS GENERAL HOSPITAL

J. C. WHITE and associates—2. Symposium: Neurological surgery.

J. C. WHITE and J. J. MICHELSEN—2. Operations.

W. J. MIXTER—4. Electro-encephalographic control of anticonvulsant therapy.

C. S. KUBIK and A. O. HAMPTON—4. Removal of lipiodol by lumbar puncture.

J. C. WHITE—4. Effect of anesthesia on volume of brain.

*Tuesday*

## MASSACHUSETTS GENERAL HOSPITAL

J. C. WHITE and associates—9. Operative and dry clinic:

W. J. MIXTER and J. S. HODGSON—9. Operations.

J. C. WHITE—11. Presentation of operative results in angina pectoris and extrapyramidal tremors.

J. J. MICHELSEN—11. Treatment of torticollis by alcohol injection of cervical muscles.

J. C. WHITE and associates—2. Dry clinic:

W. J. MIXTER. Protrusion of nucleus pulposus in cervical spine.

J. S. HODGSON. Experience with cerebellar hemangiomas (Lindau's disease).

J. J. MICHELSEN. Subdural abscess.

W. H. SWEET. New methods for measurement of blood flow.

J. C. WHITE. Spinothalamic tractotomy in the medulla.

*Wednesday*

## BOSTON CITY HOSPITAL

DONALD MUNRO and associates—9. Symposium: Injuries of the central nervous system and allied conditions.

DONALD MUNRO—9. Treatment of compound fracture of the skull, a study of 175 cases.

WALTER WEGNER—9:20. Concomitant cerebral tumors and craniocerebral injuries.

TIMOTHY LEARY—9:40. Pathology of craniocerebral injuries, with demonstration of specimens.

DONALD MUNRO—10:40. Study of 300 consecutive intracranial subdural hematomas.

WALTER WEGNER—11. Care of bone damage in cervical spinal cord injuries.

DONALD MUNRO—11:15. Present-day tidal drainage of the urinary bladder.

C. W. ELKINS—11:30. Two-needle oxygen spinograms with improved visualization of the spinal subarachnoid space.

DONALD MUNRO—11:45. Study of end-results in 130 cases of all levels of spinal cord injury.

DONALD MUNRO—12 10. Spinothalamic tractotomy in the medulla, intradural differential section of the sensory root of the fifth cranial nerve and other procedures of use in dealing with intractable pain in the head, face, mouth, neck, and arms.

DONALD MUNRO—12 20. Differential diagnosis and treatment of Ménière's disease and aural vertigo

DONALD MUNRO—12 30. Prophylaxis and treatment of pressure bed sores.

#### Thursday

##### CHILDREN'S HOSPITAL

F. D. INGRAHAM and associates—9. Symposium. Neurological surgery of children

F. D. INGRAHAM—9. Neurosurgical problems of infancy and childhood

BROWNSON CROTHERS—9 30. Definition of recovery in terms of growth and development.

F. D. INGRAHAM—9 45. Congenital anomalies requiring surgical treatment

F. D. INGRAHAM—10 15. Technical aids in neurosurgery of infancy and childhood.

BROWNSON CROTHERS—10 30. Reliability of encephalography in infancy

F. D. INGRAHAM—10 45. Presentation of cases

SYDNEY FARRER—11. Pathological aspects

F. D. INGRAHAM—11 30. Excision of premotor cortex for athetosis.

F. D. INGRAHAM—12. Subdural hematomata

##### NEW ENGLAND DEACONESS HOSPITAL

GILBERT HORRAX and associates—2. Operations

GILBERT HORRAX. Ventriculogram and craniotomy for brain tumor

J. L. POPPEN. Herniated intervertebral disc.

#### Friday

##### NEW ENGLAND DEACONESS HOSPITAL

GILBERT HORRAX and associates—9. Dry clinic

J. L. POPPEN—9. Results in herniated intervertebral discs, operations with and without fusions

J. L. POPPEN—9 30. Platysmia demonstration

GILBERT HORRAX—10. Experiences and results with brain tumors for the last 8 years

## OTORHINOLARYNGOLOGY

#### Monday

##### NEW ENGLAND BAPTIST HOSPITAL

F. D. LATIROP—1 30. Operations

##### NEW ENGLAND DEACONESS HOSPITAL

W. B. HOOVER and F. D. LATIROP—2 30. Local anesthesia in tonsillectomy, adenoidectomy, lingual tonsillectomy, and excision of lateral pharyngeal bands, septum, sinus surgery—Caldwell Luc, external frontal, intranasal, plastic procedures, external nose.

##### NEW ENGLAND MEDICAL CENTER

(Joseph H. Pratt Diagnostic Clinic—Boston Dispensary)

GEORGE KALFMAN—2. Pathogenesis of traumatic cholesteatoma, lantern slides, surgery of the tonsil after middle life, pathways of infection in the ear, lantern slides.

PHILIP E. MELTZER—2. Surgical anatomy of the temporal bone

#### Tuesday

##### BOSTON CITY HOSPITAL

Staff—9. Dry clinic

F. J. MONAHAN—9 30. A method of the extirpation of bronchial cysts.

OSCAR HIRSCH—9 50. Cysts of pituitary body

LOUIS M. FREEDMAN—10 10. Bronchoscopic treatment of pulmonary atelectasis.

CHESTER R. MILLS—10 30. Osteomyelitis of the frontal bones.

BENJAMIN RISEMAN—10 50. Gumma of nasopharynx and lung

SAMUEL W. GARFINKL—11 10. Treatment of fractures of the jaw.

PHILIP E. A. SHERIDAN, CHARLES DEWOLFF and FREDERICK HEDMICK—11 30. Presentation of cases

##### CHILDREN'S HOSPITAL

Staff—9 30. Dry clinic

CHARLES F. BERGSON. Acute laryngotracheal bronchitis: report and statistical study of 45 cases

C. G. FLAKE. Congenital anomalies of the tracheal bronchial tract, treatment of choanal atresia

C. G. FLAKE and CHARLES F. FERGLSON. Chemotherapy in upper respiratory infections of children

##### MASSACHUSETTS EYE AND EAR INFIRMARY

Staff—2 30. Dry clinic

A. S. MACMILLAN. Interpretation of sinus x rays

L. G. RICHARDS. Problems in bronchoscopy

C. T. PORTER. Orbital abscess, diagnosis and treatment

L. A. SCHALL. Cancer of the nose and sinuses

##### MASSACHUSETTS MEMORIAL HOSPITALS

Staff—2. Operative clinic

HAROLD L. BARCOCK. Mastoidectomy

BARNET WEISS. Radical sinus operation

LEIGHTON F. JOHNSON. Fenestration for otosclerosis.

##### NEW ENGLAND BAPTIST HOSPITAL

WALTER B. HOOVER—9. Operations

F. D. LATIROP—1 30. Operations.

##### NEW ENGLAND DEACONESS HOSPITAL

WALTER B. HOOVER—9. Operations.

F. D. LATIROP—1 30. Operations.

##### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

ELIZABETH DEBLOIS, ISABELLE D. KERR, MARGARET NOYES KLEINFELT, and MARY F. VASTY—10. Demonstration. Use of the audiometer

##### ST. ELIZABETH'S HOSPITAL

JOHN E. BURNS—9. Operative clinic. Radical frontal sinus, radical mastoidectomy

##### UNITED STATES NAVAL HOSPITAL

CHARLES H. ALLMAN—9. Dry clinic. Bronchoscopy for bronchiectasis, pulmonary abscess and postoperative atelectasis, synopsis of case histories and results

DAVID P. CORDRAY—9. Operations

*Wednesday*

## MASSACHUSETTS EYE AND EAR INFIRMARY

Staff—2:30. Dry clinic:

G. B. FRED. Osteomyelitis of the frontal bone.

H. G. TOBEY. Allergy, otolaryngological considerations.

P. E. MELTZER and C. I. JOHNSON. The fenestration operation.

RUTH GUILDER. The deaf child.

A. S. MACMILLAN. Interpretation of mastoid x-rays.

## MASSACHUSETTS MEMORIAL HOSPITALS

LEIGHTON F. JOHNSON—2. Dry clinic: Mediastinitis, 3 cases, 2 cures (with Howard M. Clute); endaural repair of postauricular fistula, 3 cases; osteomyelitis of frontal bone; Lempert's operation, endaural fenestration for otosclerosis; ears in contagious diseases (with Conrad Wesselhoeft).

## NEW ENGLAND BAPTIST HOSPITAL

WALTER B. HOOVER—9. Operations.

F. D. LATHROP—1:30. Operations.

## NEW ENGLAND DEACONESS HOSPITAL

WALTER B. HOOVER—9. Operations.

WALTER B. HOOVER and F. D. LATHROP—2:30. Dry clinic: Diseases of the esophagus, summary of symptoms, diagnosis and treatment; carcinoma; cardiospasm; esophageal diverticulum; esophagitis; ulcers, strictures and perforation of the esophagus.

*Thursday*

## BETH ISRAEL HOSPITAL

Staff—9. Dry clinic:

SAMUEL CLINE. Tuberculous laryngitis.

OSCAR HIRSCH. Sphenoid approach through submucous septum.

A. J. GORNEY. Lempert's simple and radical mastoid operations.

S. W. GARFIN. Transseptal approach for dacryocystitis.

H. F. FRIEDMAN. Radiation for carcinoma of larynx by the Coutard method.

BENJAMIN RISEMAN. Cavernous sinus thrombosis.

LOUIS M. FREEDMAN. Coutard radiation therapy for carcinoma of larynx, end-results; Lempert technique for simple and radical mastoidectomy.

LOUIS M. FREEDMAN. Lempert operation for mastoiditis.

## BOSTON CITY HOSPITAL

Staff—9. Operations.

## CARNEY HOSPITAL

BENJAMIN E. RISEMAN—2. Edema of larynx with abscess.

CORNELIUS S. HICKEY—2. Mastoiditis with complications.

## MASSACHUSETTS EYE AND EAR INFIRMARY

Staff—9. Operations.

Staff—2:30. Dry clinic:

L. A. SCHALL. Laryngeal cancer.

V. H. KAZANJIAN. Rhinoplastic surgery.

PHILIP MYSEL. Labyrinthectomy, review of cases.

C. M. KOS. Meningitis, review of cases and discussion.

## NEW ENGLAND BAPTIST HOSPITAL

WALTER B. HOOVER—9. Operations.

F. D. LATHROP—1:30. Operations.

## NEW ENGLAND DEACONESS HOSPITAL

WALTER B. HOOVER—9. Operations.

NEW ENGLAND HOSPITAL FOR WOMEN  
AND CHILDREN

ELIZABETH DEBLOIS, ISABELLE D. KERR, MARGARET NOYES KLEINERT, and MARION C. SABIA—9. Operations.

Staff—10. Demonstration: Use of the audiometer.

## ST. ELIZABETH'S HOSPITAL

WILLIAM T. HALEY—9. Operations.

*Friday*

## BETH ISRAEL HOSPITAL

Staff—9. Operations.

## CARNEY HOSPITAL

BENJAMIN E. RISEMAN and staff—9. Operative clinic.

## MASSACHUSETTS MEMORIAL HOSPITALS

Staff—9. Operations.

## NEW ENGLAND BAPTIST HOSPITAL

WALTER B. HOOVER—9. Operations.

F. D. LATHROP—1:30. Operations.

## NEW ENGLAND DEACONESS HOSPITAL

WALTER B. HOOVER—9. Operations.

F. D. LATHROP—1:30. Operations.

NEW ENGLAND HOSPITAL FOR WOMEN  
AND CHILDREN

ELIZABETH DEBLOIS, ISABELLE D. KERR, MARGARET NOYES KLEINERT, and MARION C. SABIA—9. Operations.

ESTHER E. BARTLETT—10. Operations under endotracheal anesthesia.

## NEW ENGLAND MEDICAL CENTER

(Boston Floating Hospital)

W. A. MCCOLL—2. Adenoid and tonsil problems.

# SURGERY, GYNECOLOGY AND OBSTETRICS

## OPHTHALMOLOGY

### Monday

MASSACHUSETTS EYE AND EAR INFIRMARY  
F. H. VERHOEFF and WILLIAM P. BEETHAM—2 15 Dry  
Clinic—Cataract surgery.

Scientific Exhibit—Daily  
T. L. TERRY Pathological laboratory open for inspection  
DAVID G. COGAN Howe laboratory and library open

### Tuesday

BOSTON CITY HOSPITAL  
JAMES J. REGAN and staff—9 Abnormal fundi.

UNITED STATES NAVAL HOSPITAL  
JAMES J. REGAN—9 Demonstrations of technique used  
in flight physical examinations, with discussions of  
United States Naval requirements.  
VIRGIL G. CASTEN—10.30 Operations

MASSACHUSETTS EYE AND EAR INFIRMARY  
PAUL A. CHANDLER, FRID S. THORNE, TRYGVE GUNDER-  
SEN, and PAUL G. HAIRE—9 Operations  
WILLIAM P. BEETHAM—9 Demonstration Slit lamp  
PAUL A. CHANDLER—2 15 Dry clinic Glaucoma, indica-  
tions for operation  
SAMUEL T. CLARKE—3 15 Dry clinic Goniotomy, medi-  
cal treatment of glaucoma

### Wednesday

MASSACHUSETTS EYE AND EAR INFIRMARY  
WILLIAM P. BEETHAM, SAMUEL H. WILKINS, BRENDAN D.  
LEAHEY, and DAVID G. COGAN—9 Operations.  
GARRETT L. SULLIVAN—9 Demonstration Perimetry.  
E. B. DUNPHY—2 15 Strabismus, orthoptic training  
VIRGIL G. CASTEN—3 15 Dry clinic Strabismus, opera-  
tive treatment

MASSACHUSETTS MEMORIAL HOSPITALS  
WILLIAM D. ROWLAND—9.30 Dry clinic

### Thursday

BOSTON CITY HOSPITAL  
JAMES J. REGAN and staff—9 Operations.

CARNEY HOSPITAL  
GEORGE GAGLIARDI—2 Dry clinic: Suture and cataract  
extraction.  
LEROY FORD—2 Dry clinic: Orbital abscess in children  
SAMUEL T. CLARKE—2 Contact lenses

MASSACHUSETTS EYE AND EAR INFIRMARY  
EDWIN B. GOODALL, RALPH H. RUGGLES, MERRILL J.  
KING, and HERMAN GROSSMAN—9 Operations  
VIRGIL G. CASTEN—9 Demonstration Neuro-ophthal-  
mology.  
MERRILL J. KING—2 15 Dry clinic Retinal separation  
BRENDAN D. LEAHEY—3 15 Dry clinic Keratoplasty

MASSACHUSETTS MEMORIAL HOSPITALS  
WILLIAM D. ROWLAND, JOSEPH J. SKIRBALL, EDWARD L.  
PERRY, and RALPH H. HOPKINS—2 Operative clinic.  
Cataract, glaucoma, and muscles

ST ELIZABETH'S HOSPITAL  
HUGH DONAHUE—10 Operations Cataract extraction,  
decompression operation for primary glaucoma

### Friday

CARNEY HOSPITAL  
SAMUEL T. CLARKE and staff—9 Operative clinic.

MASSACHUSETTS EYE AND EAR INFIRMARY  
BENJAMIN SACHS and JOHN C. JENNINGS—9 Operations  
Staff—9 Demonstrations  
SAMUEL T. CLARKE Gonioscopy  
T. L. TERRY—2 15 Dry clinic and lantern demonstra-  
tions of pathological specimens  
V. H. KAZANJIAN—3 15 Dry clinic Ophthalmoplastic  
surgery.





Fig 20 Case 4. Large subcostal opening after removal of herniated colon  
Sac of peritoneum containing round ligament extending into thoracic cavity

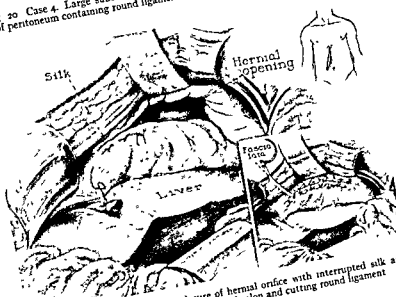


Fig 21 Case 4. Overlapping closure of hernial orifice with interrupted silk and continuous fascia lata sutures after removal of colon and cutting round ligament

# SURGERY

## GYNECOLOGY AND OBSTETRICS

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### SUBCOSTOSTERNAL DIAPHRAGMATIC HERNIAS

#### Foramen of Morgagni

STUART W. HARRINGTON, M.D., F.A.C.S., Rochester, Minnesota

ONE of the weak regions in the structure of the diaphragmatic muscle as well as one of the weaker attachments of this muscle to the chest wall occurs in the middle leaflet of the diaphragm anteriorly, where, on either side of the sternal attachment in the midline, there are too small apertures caused by deficiencies in the structure of its musculature. These spaces devoid of muscle are triangular with the apex toward the central tendon and the base at the costal margin between the xiphoid process and the pars costalis which starts at the inner surface of the six lower ribs. In some instances the sternal attachment of the diaphragm may be absent or defective, so that the two spaces may fuse into one large opening beneath the sternum and sternocostal junction. These spaces are covered on the thoracic side by pleura and on the abdominal side by the diaphragmatic peritoneum. They are filled with loose areolar tissue and through these spaces pass the superior epigastric artery and lymphatics. These spaces in the anterior portion of the diaphragmatic muscle are called Larrey's spaces and foramen of Morgagni.

The occurrence of herniations of abdominal viscera through these weak regions into the thoracic cavity has been known for many years. Morgagni is credited with the first description of a diaphragmatic hernia of this type, in 1769, occurring in a patient whom Leprotti had seen in Rome and who died of other causes at an advanced age. At necropsy herniation of the intestine into the thoracic cavity through an opening beneath the sternocostal junction was found, but there was no obstruction of the bowel to suggest that it was a factor in the death, and no signs of injury to the diaphragm were found to indicate a traumatic origin of the hernia.

Hernias of the diaphragm occurring through these regions have received various terminologies such as diaphragmatic hernia through the foramen of Morgagni, or through Larrey's fissure or spaces, and also substernal, retrosternal, parasternal, or anterior diaphragmatic hernia. Inasmuch as these hernias usually occur to either side of the anterior midline of the diaphragm, if an anatomical terminology is to be used, it would be preferable to call them subcostosternal diaphragmatic hernia.

Although the occurrence of this type of diaphragmatic hernia has been known for many years there are relatively few cases reported in the literature as compared with

From the Division of Surgery, Mayo Clinic.  
Read before the Meeting of Western Surgical Association,  
Topeka, Kansas, December 6 and 7, 1940.



other types of diaphragmatic hernia Hedblom (1932) stated that about 60 cases had been reported and Funck-Brentano (1933) stated that 58 cases had been reported in the literature, however, neither author gave bibliographic references of the cases traced or reported. I have reviewed the literature in an attempt to trace the individual case reports and had hoped to have it completed at this time, but there are many duplications of reports and indefinite or inadequate descriptions of cases which have made it impossible to complete the study at this time.

In a review of the literature from 1930 to the present time it was found that 24 cases had been reported, in only 5 of which had operation been performed, in 2 by the abdominal approach, in 2 by the thoracic approach, and in 1 by combined abdominal and thoracic approach. Of the 5 patients on whom operation was performed, 3 were adults and 2 were children, all recovered from operation. The ages of the entire group of patients varied from 17 days to 72 years. Five patients were from 17 days to 1 year of age, 6 from 1 year to 9 years of age, 2 from 10 to 19 years of age, 3 from 20 to 29 years of age, 1 from 30 to 39 years of age, 1 from 50 to 59 years of age, 3 from 60 to 69 years of age, and 3 from 70 to 72 years of age. Thirteen patients were female and 11 were male. In 17 cases the hernia was on the right side, in 2 on the left side, in 2 it was bilateral, and in 3 cases the side was not stated. In 3 cases roentgenological examination was not done and in 1 case pulmonary cyst was diagnosed. In the 3 cases in which roentgenograms were not made, the hernia was found at necropsy. In 4 cases the roentgenological findings were confirmed at necropsy. Out of the 24 cases were proved by operation and 7 were proved by necropsy to be this type of hernia.

There is some difference of opinion as to whether these hernias should be classified as congenital or acquired hernias. It is impossible to explain their occurrence on a basis of faulty fusion or improper disposition of the embryonic mesodermic elements which go to form the diaphragm, as this anterior portion of the diaphragm is derived from the septum transversum only. But the consistency of the

location of the hernial opening, the fairly constant relation of the neck of the sac to the round and falciform ligaments of the liver, and the frequency with which the hernial sac protrudes into the right side of the thoracic cavity at the same point of entrance at the cardiophrenic angle, as well as the often associated nonrotation of the right portion of the colon, all strongly suggest a fundamental embryologic basis for these hernias. These hernias are essentially direct hernias through a congenital defect in the structure of the diaphragm or a faulty attachment of the phragm to the sternum and costal cartilages. The consistency of the presence of a peritoneal sac shows that the peritoneum had closed off the abdominal cavity from the pleural cavity before the actual herniation of the abdominal viscera occurred. The consistency of the presence of the round and falciform ligaments of the liver in the peritoneum forming the sac suggests that there may be a relationship of the occurrence of this abnormal opening at the time of the rotation of the liver to the right side of the abdomen. The infrequency of traumatic lacerations involving the anterior portion or attachments of the diaphragm also supports the probability of a fundamental congenital origin of these hernias. The larger attachment of the pericardium to the anterior left side than to the right side of the thoracic diaphragm probably accounts for their increased frequency on the right side.

It is difficult to ascertain the actual incidence of subcostosternal hernias of the diaphragm, as many cases reported have not been proved by necropsy or operation. In my experience they constitute the least common type that I have operated upon. In a series of 270 operations for various types of diaphragmatic hernia, only 4 hernias were of the subcostosternal type, while 217 were through the esophageal hiatus, 14 of which were of the short esophageal type, 9 were through structural defects in the diaphragm (5 being due to congenital absence of the posterior portion of the diaphragm and 4 being due to the peritoneal hiatus type) and 40 were due to traumatic lacerations of the diaphragm caused by either direct or indirect injury. In the latter group 39 were through the left side of

the diaphragm and 1 was through the right side. In the 4 cases of subcostosternal diaphragmatic hernia, the hernia extended into the right side of the thoracic cavity while in the 217 esophageal hiatus hernias only 23 extended markedly into the right side.

In the 4 cases of subcostosternal hernia, the location of the defect in the diaphragmatic muscle varied with the size of the opening. One was entirely to the right side of the midline and the 3 others were more to the right but extended beneath the sternum. In 1 of these the opening extended entirely beneath the sternum and slightly to the left of the midline, uniting the two foramina, there being no attachment of the diaphragm to the under surface of the sternum.

There was a complete hernial sac enveloping the herniated viscera in all 4 cases, and the round and falciform ligaments of the liver were involved in the peritoneal sac in all cases. The amount of involvement of the round and falciform ligaments in the formation of the sac depends on the size of the hernial sac and its extent into the thoracic cavity. In 3 of the 4 cases the sacs were very large and there was no remaining attachment of the round ligament to the anterior abdominal wall as it had been drawn entirely into the thorax and formed a part of the posterior or lateral opening of the sac.

Subcostosternal diaphragmatic hernia is one of the two types of diaphragmatic hernia, in my experience, which have a hernial sac. The other type of diaphragmatic hernia which has a hernial sac is that through the esophageal hiatus. It is interesting that subcostosternal hernia is probably the rarest type of diaphragmatic hernia and esophageal hiatus diaphragmatic hernia is the most common; both are essentially congenital in origin but are rarely present at birth and occur usually in later life because of increased abdominal pressure on a congenitally defective diaphragm.

The abdominal viscera involved in the hernias were omentum only in 2 cases, omentum and entire transverse colon in 1, and omentum, cecum, appendix, and part of ascending colon and terminal ileum in the fourth case.

The subjective symptoms in the 4 cases here reported varied from mild respiratory

symptoms to repeated attacks of intestinal obstruction. In 1 case there was also an esophageal hiatus hernia which caused marked gastric symptoms. These were the patient's chief complaint, and it was not thought that the subcostosternal hernia was causing definite subjective symptoms as the omentum was the only abdominal structure involved in the hernia. This patient, a woman, also had severe asthma and it is probable that the herniation of the omentum added to her respiratory difficulty. In the second case, in which omentum only was involved in the hernia, the patient, a woman, had attacks of repeated pulmonary infections with cough and expectoration and complained of progressive dyspnea, particularly in the 2 years prior to her admission, during which time she had gained 60 pounds (27.2 kilograms). Because of the enormous amount of omentum herniated into the thorax and compressing the lung, I believe that these respiratory symptoms were due to the hernia. In both the third and the fourth case, intestine was involved in the hernial sac and the symptoms were those of periodic attacks of partial intestinal obstruction and digestive disturbance often associated with epigastric pain extending into the right side of the thorax; there were also considerable gas and bloating after meals, often associated with smothering spells and dyspnea which were more marked at night, necessitating sitting up to breathe, as well as gradually increasing constipation.

In the cases in which hollow viscera are involved in the hernia symptoms occur which suggest the possibility of a hernia or at least the necessity of a roentgenological examination of the intestinal tract which will show the presence of a hernia. The cases in which omentum only is involved in the hernia present a much more difficult clinical problem in arriving at a definite diagnosis. The subjective symptoms in the latter group are entirely thoracic as a result of mechanical interference with respiration and expansion of the lungs. These symptoms suggest a primary pulmonary lesion and direct the clinical investigation to roentgenological study of the thorax. The roentgenological findings of an increased density in the pulmonary field justify the

clinical diagnosis of a primary intrathoracic lesion which may be thought to be an intrathoracic tumor. This erroneous clinical diagnosis is particularly likely to occur if there are no subjective symptoms even to suggest that an abdominal condition may be present, and even though the gastrointestinal tract is examined roentgenologically no lesion is demonstrated as no abdominal viscera are involved in the hernia.

This, I believe, is the most important clinical consideration in this group in which the omentum is the only abdominal structure involved in the hernia. In the 2 cases here reported of this type the patients were both sent to the Mayo Clinic with a diagnosis of intrathoracic tumor. The true diagnosis was not established until the time of the operation. In the first case there was also a pharyngeal hiatus hernia for which operation was advised and the subcostosternal omental hernia was found upon exploration. In the second case the true diagnosis was established by exploratory thoracotomy, although an omental subcostosternal diaphragmatic hernia was considered as a possibility before thoracotomy, however, upon roentgenological examination of the gastrointestinal tract it was found to be negative. The possibility of a subcostosternal diaphragmatic hernia was considered because of the roentgenological findings of a rounded shadow situated anteriorly, originating at the right cardiophrenic angle, the contour of the density was not completed in the thoracic cavity. I should like to emphasize the difficulties which may be associated with establishing a definite diagnosis of omental subcostosternal diaphragmatic hernia and the possibility that such a hernia may be diagnosed uncommonly as a primary intrathoracic lesion.

The treatment of subcostosternal diaphragmatic hernia is surgical closure of the abnormal opening in the diaphragm after replacement of the herniated abdominal viscera into the abdomen.

The indications for surgical intervention depend to some extent on the type of abdominal viscera involved in the hernia. In those cases in which hollow abdominal viscera are involved in the hernia, immediate surgical

intervention is demanded because the danger of incarceration, obstruction, and strangulation is imminent. In cases in which it is definitely proved that the omentum is the only abdominal structure involved, operation may be delayed for reduction of weight or improvement of the patient's condition, but these patients should be carefully observed during the preoperative preparation as, with reduction in weight, the colon may be drawn into the hernial sac and immediate operation required.

The approach should be through an abdominal upper right rectus incision because the opening in the diaphragm is very accessible from the abdominal side. From the thoracic side the opening is difficult to expose as it is obscured by the right pericardial attachments to the diaphragm and access is difficult because of the contour of the right border of the pericardium which is above the opening and lateral to it.

The abdominal contents of the hernia are more safely and easily reduced from the abdominal side as the true relationship of the herniated viscera to the hernial sac can be accurately determined and any injury to these structures can be easily recognized and quickly repaired.

The treatment of the hernial sac depends on its size and on the relationship of the round and falciform ligaments of the liver to the sac. The true neck of the sac is usually to the left side of the round ligament which is pushed to the right of the midline. If the sac is small, it can be completely removed and excised and the opening in the diaphragm closed without disturbing the round ligament. If the sac is large it is best to leave it *in situ*, cut the round ligament so there will be no tendency to drag the margin of the liver up, and utilize the round ligament to strengthen the closure at the neck of the sac. If a large sac is left *in situ*, it is well to make several incisions through the peritoneum of its wall to prevent the accumulation of fluid in the sac after the neck of the sac has been closed.

The method of closure of the neck of the sac and of the defect in the structure of the muscle of the diaphragm depends on the size and character of the opening. Small linear openings may be closed by overlapping the

margins. Larger transverse openings extending beneath the sternum are best closed by suturing the anterior margin of the diaphragmatic muscle defect to the posterior sheath of the rectus muscle and anterior chest wall.

The most satisfactory material for closure of the opening is living suture of fascia lata removed from the thigh and stabilized in the tissues with silk. The round ligament of the liver can be incorporated in this closure to strengthen it as well as to re-establish its position on the anterior abdominal wall.

The closure of the large openings is facilitated by paralyzing the right side of the diaphragm by temporary interruption of the right phrenic nerve. This procedure, however, is not necessary in the closure of small openings. Preparation can be made to interrupt the phrenic nerve in the supraclavicular region after the opening is explored and it is determined whether or not interruption is necessary.

The operative approach for the repair of the subcostosternal hernia in the 4 cases which I am reporting, was abdominal in all instances. The sac was removed in 2 cases and was left *in situ* in 2. The herniated viscera were reduced and the opening was repaired in all 4 cases. There were no operative deaths and no subsequent recurrence of the hernias.

#### REPORT OF CASES

CASE 1. A woman, aged 64 years, consulted the Mayo Clinic on June 25, 1932, because of a diagnosis of intrathoracic tumor on the right side. Her chief complaints were asthmatic attacks with dyspnea on exertion, intermittent attacks of stomach trouble, loss of weight and strength, and insomnia. With the exception of numerous irregular attacks of asthma for a period of more than 30 years, more severe in the spring and fall, she always had enjoyed good health until 4 years before her admission when she first noticed difficulty in the swallowing of food and at times she would spit up some food immediately after eating. This, however, was not associated with pain. This condition continued for about 5 months after which a roentgenogram of the stomach was taken and a diagnosis of ulcer and dilatation of the cardia of the stomach was made. Medical management for ulcer was begun, and the patient obtained complete relief of symptoms until 3 years before her admission to the clinic when following an attack of pyelitis, severe symptoms similar to the previous attack again developed. She was again relieved by medical treatment.

Three months prior to her admission to the clinic the patient had a recurrence of her digestive symptoms with spitting up of food and mucus and with epigastric distress most marked at night. Some relief was obtained from taking soda and restricting her diet to frequent small feedings. Roentgenograms of the stomach were taken again, and the patient was told that the ulcers which had been visualized at the previous examination were completely healed but that the roentgenograms of the lungs revealed an intrathoracic tumor on the right side. The patient gave no history of injury.

On physical examination her blood pressure was 128 millimeters of mercury, systolic, and 80, diastolic. Her weight was 112 pounds (50.8 kilograms). An examination of her chest showed emphysema, grade 2, on a basis of 1 to 4, and there were scattered râles of an asthmatic condition to be heard. Her fingers were clubbed, but she said this condition had always been present. Urinalysis showed an occasional pus cell, but the results were otherwise negative. The hemoglobin was 13.3 grams per 100 cubic centimeters of blood; erythrocytes numbered 4,380,000 and leucocytes 5,100 in each cubic millimeter of blood. The flocculation reaction was negative. The roentgenogram taken of the chest and stomach revealed a large tumor at the base of the right lung anteriorly, and herniation of the cardiac end of the stomach through the esophageal hiatus with a third of the stomach above the diaphragm.

Because of the preponderance of gastric symptoms, operation for the esophageal hiatus hernia was advised, and this was done on June 29, 1932, through an abdominal incision under intratracheal ethylene and ether anesthesia. Upon exploration of the abdomen, the omentum was found to pass over the dome of the left lobe of the liver and entered the right side of the thoracic cavity through an opening close to the anterior attachments of the diaphragm just to the right of the ensiform cartilage. The omentum was the only abdominal structure which passed through the opening. The transverse colon was slightly elevated but it was not involved in the hernia. It was the presence of the omentum in the right side of the thoracic cavity which produced the roentgenological shadow which was thought to be an intrathoracic tumor. The omentum was moderately adherent to the hernial sac but was removed without difficulty. The opening in the anterior surface of the diaphragm was somewhat linear, being about 3 inches (8 centimeters) in length along the costal margin, extending to the sternum, and about 1 inch (2.5 centimeters) in width. The hernial sac consisted of peritoneum and was just to the left of the round and falciform ligaments of the liver. There was a complete peritoneal sac which was about 5 inches (13 centimeters) in depth.

This sac was inverted and excised and the peritoneum was closed with the closure of the hernial opening in the structure of the diaphragm by overlapping the margins for a distance of 2 centimeters. Examination of the stomach revealed an enlarged

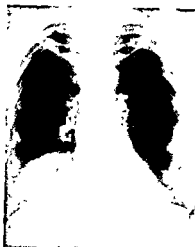


Fig 1.

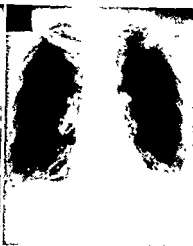


Fig 3



Fig 4



Fig 5

Fig 1 Case 1 Subcostal hernia on admission. Large, rounded shadow right lower part of thorax, obscuring right border of heart and lung field.

Fig 3 Case 1 Six months after operation. Right lung entirely expanded. Diaphragm, heart, and lung fields negative.

Fig 4 Case 1 Herniation of cardiac end of stomach through esophageal hiatus, also on admission.

Fig 5 Case 1 After repair of esophageal hiatus hernia, showing stomach in normal position below diaphragm. Operation performed at same time as that shown in Figure 2.

esophageal hiatus which was about 10 centimeters in diameter, through which about a third of the cardiac end of the stomach had herniated into the posterior mediastinum. The hernial sac was cut from its attachments to the stomach and permitted to retract into the posterior mediastinum. After replacement of stomach into abdomen, enlarged esophageal hiatus was repaired by overlapping from above downward, innermost suture of the repair proximal to esophagus incorporated the loose areolar tissue and remnants of peritoneal sac in the lower esophagus in the closure, fixing it to the inner margin of repaired hiatus. Stomach and duodenum did not show any intrinsic lesion (Figs 1 to 5).

The patient's convalescence was uneventful and she was dismissed from the hospital on the twenty-first day. Her general condition was good and her wound completely healed. The roentgenogram of the stomach revealed it to be in normal position below the diaphragm and she had no gastric complaint. The roentgenogram of her lungs was normal with no evidence of the shadow in the right lower anterior portion of the chest which had been thought to be due to an intrathoracic tumor before operation.

This case is of particular interest from both a clinical and a surgical standpoint. The patient's clinical symptoms presented a dual

type of complaint. The chief complaint of loss of weight and strength and the associated asthmatic attacks with clubbing of fingers and scattered râles throughout the lungs, suggested a primary pulmonary lesion which was somewhat substantiated by the roentgenological findings of a shadow diagnosed as a tumor in the right side of the thoracic cavity. The other phase of her clinical symptoms was that of the gastric complaint which consisted of nausea, vomiting, and epigastric distress, occurring about 2 hours after meals but often noted before the patient had finished her meal. The pain was more marked at night and was relieved by belching of gas or vomiting. This phase of her complaint was fairly characteristic of an esophageal hiatus diaphragmatic hernia with an associated traumatic ulcer, as the symptoms of this condition often simulate those of a gastric ulcer.

The surgical indication in this case presented a problem as to the method of approach. I decided that the esophageal hiatus diaphragmatic hernia was responsible for the major portion of the patient's symptoms and probably for the loss of weight owing to the inability to take food. I felt, therefore, that the stomach should be explored first and that there was a possibility that the shadow in the anterior mediastinum might be an anterior type of hernia rather than a primary tumor of the lung. The discovery at operation of an esophageal hiatus diaphragmatic hernia and of anterior herniation of the omentum through the foramen of Morgagni is very unusual. In a series of 270 cases of diaphragmatic hernia in which I have operated, this is the only case in which there were two distinct congenital types of hernia through the diaphragm. This case exemplifies the importance of considering the herniation of the abdominal viscera or omentum through the diaphragm in the event of an abnormal shadow in the lower part of the thorax. I know of no other case reported in the literature which presented two separate and distinct congenital hernial openings with herniation of abdominal viscera through the diaphragm.

**CASE 2.** A woman, aged 46 years, consulted the clinic on February 1, 1939, because of persistent productive cough of more than 2 years' duration.

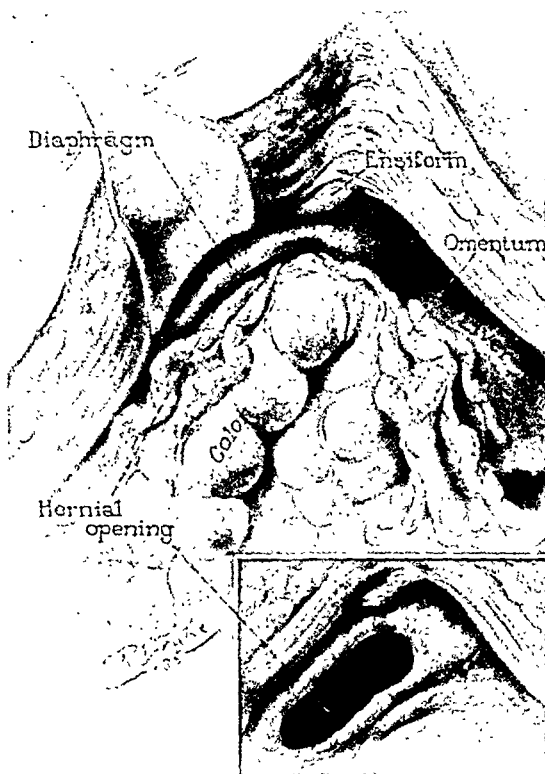


Fig. 2. Case 1. Operation by abdominal approach. Herniation of omentum and colon through opening to right of ensiform cartilage.

She had been subject to "head colds" for the past 10 years. These had become more frequent and severe since she had put on weight. She had gained 60 pounds (27.2 kilograms) in the past 2 years and on admission weighed 190 pounds (86.2 kilograms). At first there was relatively little expectoration associated with the cough, but following a severe "cold" about a year ago the patient began coughing up "greenish material that looked like pus." Since that time the cough had been productive but the sputum changed to mucoid material and amounted to about 1 cupful a day. The patient coughed mostly at night and often throughout the night and obtained some relief upon sitting up. She recently had had severe night sweats. Her voice had become husky and hoarse most of the time. Hemoptysis was not noted. She had had moderate dyspnea, more marked on exertion. Chest pain was not present. Appetite was excellent. The patient had no symptoms referable to the gastrointestinal tract. There was no history of injury. She was referred to the clinic with a clinical diagnosis of intrathoracic tumor.

On physical examination her blood pressure was 135 millimeters of mercury systolic and 85 diastolic. Examination of the thorax revealed decreased



Fig 6



Fig 7.

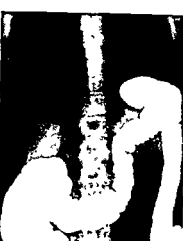


Fig 8.

Fig 6 Case 2 Anteroposterior view on admission. Dense rounded tumor right lower part of thorax. Pre-operative diagnosis was benign tumor or encysted fluid.

Fig 7 Case 2 Lateral view on admission. Shows that

fremitus, diminished breath sounds and dullness to percussion over the lower area of the right lung. Urinalysis showed pus, grade 1, but the results were otherwise negative. The hemoglobin was 13.8 grams per 100 cubic centimeters of blood and leucocytes numbered 7,400 in each cubic millimeter of blood. Flocculation reaction was negative. X-ray examination of thorax showed a homogeneous opacity over lower and anterior fields of right lung, thought to be a benign tumor or encysted fluid (Figs. 6, 7).

Although there were no abdominal symptoms, the position of the shadow in the right side of the thoracic cavity originating at the cardiophrenic angle anteriorly suggested the possibility of a subcostosternal hernia, and the entire gastrointestinal tract was examined roentgenologically but found to be normal (Fig 8). The clinical diagnosis was intrathoracic lesion, probably tumor, and exploration was advised.

A right artificial pneumothorax was done preliminary to the operation and roentgenograms taken after this procedure did not give any additional information as to the lesion. The transpleural exploration of the right side of the thoracic cavity was carried out on February 15, 1939. The seventh rib was resected and upon exploration of the thorax a large tumor mass was found originating from the right cardiophrenic angle of the lower right side of the thoracic cavity and extending entirely behind the mediastinal and anterior parietal pleura to the hilum of the right lung superiorly and to the mid-portion of the right side of the thoracic cavity laterally. This anterior mass occupied a third of the entire right side of the thoracic cavity, compressing the lower and middle lobes of right lung posteriorly. The pressure had produced adhesions between the parietal and visceral pleura around the mass.

dense rounded tumor is located anteriorly, completely obscuring heart shadow.

Fig 8 Case 2. On admission. Entire colon in normal position below diaphragm.

After separation of these adhesions and section of the pleura the mass was found to be a peritoneal hernial sac coming through an opening in the anterior portion of the diaphragm just beneath the costosternal junction. The peritoneal sac was opened and was found to contain an enormous omental fat apron. It was impossible to replace this herniated omentum through the relatively small hernial orifice owing to the fixation of the omentum at the neck of the sac which was angulated beneath the right border of the heart. It is possible that replacement might have been accomplished by enlarging the opening in the diaphragm, but I did not think this procedure was advisable, as the patient was very obese and there was no space in the abdominal cavity to receive this huge omental mass. I did not think it advisable to enlarge the opening because of the danger of injury to the colon, and it was thought best to close the thoracic cavity as an exploration and to replace the herniated omentum through an abdominal approach at a later operation after the patient's weight had been reduced.

The patient made a good recovery from the exploratory thoracotomy and was permitted to return home on a reduction diet. She returned to the clinic in 3 months, having lost 50 pounds (22.7 kilograms). Her general condition was very satisfactory. On June 17, 1939, the right subcostosternal hernia was repaired under cyclopropane anesthesia, through an upper right rectus abdominal approach.

On exploration of the abdomen a relatively large subcostosternal opening through the right anterior portion of the diaphragm was found. The opening was mostly on the right side but also extended beneath the sternum and slightly to the left of the midline. It was somewhat kidney shaped because the

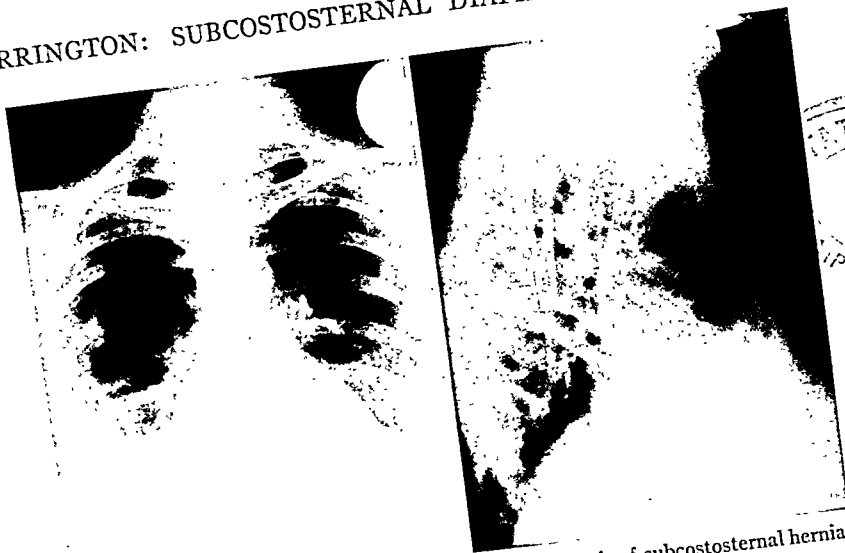


Fig. 9, left. Case 2. Anteroposterior view. After repair of subcostosternal hernia. Lung almost completely expanded. Small amount of fluid in residual sac.  
Fig. 10. Case 2. Lateral view after repair of hernia.

falciform and round ligaments of the liver were contained in the hernial sac posteriorly. The hernial sac consisted of peritoneum; the neck of the peritoneal hernial sac extended into the thorax and was angulated upward and forward. The peritoneal opening was to the right of the midline but to the left of the round and falciform ligaments of the liver. There was a depression in the peritoneum to the right of the round ligament, but it was impossible to pass a finger into the hernial sac to the right of this ligament. The entire omentum had herniated through this opening and was quite adherent to the margins of the opening of the sac.

The omentum was entirely separated from its attachment to the neck and from the sac itself and replaced into the abdomen. The falciform and round ligaments were then cut away from their attachments to the hernial sac so as to sever their continuity with the sac and permit a more accurate closure of the neck of the sac. Because of the huge size of the sac, which extended high into the thoracic cavity, and its known fixation to the lung, no attempt was made to remove the entire sac. Several incisions were made into the wall of the sac to prevent accumulations of fluid in the sac. The hernial orifice and neck of the sac were then closed by overlapping the left side over the right side for at least 1.5 to 2 centimeters. The closure was made with a continuous suture of fascia lata which had been moved from the right thigh and the fascia was fixed into this overlapped closure with interrupted linen sutures. The cut round and falciform ligaments were then sutured over this closure to reinforce it as well as to re-establish normal position of round ligament to its attachment to abdominal wall and aid in obliterating this space above liver to prevent entrance of abdominal viscera to this region.

A transfusion of blood was given immediately after the operation. The patient's convalescence was uneventful. The patient was dismissed from our care about 4 weeks from the time of operation, at which time the wound was entirely healed. Her general condition was very satisfactory. The roentgenogram of the thorax revealed that the hernial sac was obliterated completely. There was still increased density over the right lower part of the thorax from thickened pleura resulting from the previous thoracotomy wound (Figs. 9 and 10). The patient returned to the clinic for a recheck of her condition 1 year after repair of hernia. She was in excellent health and had no subjective symptoms. The roentgenograms revealed small interlobar pleuritic bands in right lower thorax. The lung fields were normal. There was no recurrence of the hernia.

This case is interesting because of the difficulties encountered in establishing a clinical diagnosis, which resulted in the necessity of two operative procedures in order to effect a cure of the condition. Although the possibility of a subcostosternal hernia was suspected, this preoperative diagnosis could not be established. The entire gastrointestinal tract was examined roentgenologically before operation and it was found that the stomach and the colon were in normal position and there was no evidence of any deviation from their normal position to suggest herniation of these viscera or of the omentum. Inasmuch as one of the patient's subjective symptoms suggested an intrapulmonary or intrathoracic



lesion, and as this suggestion was substantiated by clinical and roentgenological findings, exploratory thoracotomy was indicated.

The case is also of interest because of the difficulty encountered in attempting to replace the herniated omentum from the thoracic approach. Two courses could have been followed. The omentum could have been excised and the opening in the diaphragm could have been enlarged but because of the extreme obesity of the patient and the fact that the omentum had lost its right of residence in the abdomen as well as the possibility of injury to the colon, these procedures were not thought advisable. A certain hazard was taken in permitting the patient to return home because of the possibility of the colon becoming involved in the hernia, particularly following reduction in weight and decrease in the fatty omental content of the hernial sac, as the only reason that the colon had not become involved in the hernia was that the sac was completely filled with omentum. The patient was cautioned on her first dismissal that if she experienced any abdominal symptoms she should return for operation without any further delay. The ultimate satisfactory result obtained from the abdominal reduction and repair of the hernia was very gratifying.

**CASE 3** A man, aged 27 years, consulted the clinic on June 6, 1940, because of irregular periodic attacks of abdominal distress and bloating of 7 years' duration. He stated that he had always been in excellent health until the onset of these symptoms. He had noticed that his abdomen would become distended after meals. This distention was associated with generalized abdominal distress which had recently reached a degree of severe pain. The pain was most severe when he lay down at night. On several occasions he had had a smothering sensation which would be relieved by sitting up. He would have nausea following meals but had never vomited. He had noticed gurgling in the abdomen which would extend into the lower part of the chest. He had become increasingly more constipated, requiring the constant use of laxatives. His general condition had remained satisfactory except for weakness and loss of weight. There had been no history of injury.

On physical examination the patient was found to weigh 116 pounds (52.6 kilograms). His normal weight was 138 pounds (62.6 kilograms). The loss of weight extended over a period of 7 years. Examination of the abdomen revealed slight generalized tenderness. Examination of the chest revealed a percussion note under the sternum, rather tympanic.

The blood pressure was 152 millimeters of mercury systolic and 80 diastolic. Urinalysis revealed an occasional erythrocyte and an occasional pus cell, but the results were otherwise negative. The hemoglobin was 14.4 grams per 100 cubic centimeters of blood, erythrocytes numbered 5,160,000, and leucocytes 7,300 in each cubic millimeter of blood. The flocculation reaction was negative. The roentgenological examination of the thorax was reported as giving negative results. The roentgenological examination of the colon revealed herniation of the cecum and ascending colon as well as a portion of the terminal ileum through an opening in the anterior right side of the diaphragm with the aforementioned portions of the bowel lying in the anterior mediastinum slightly to the right of the midline and just to the right and posterior to the lower part of the sternum and the xiphoid process (Figs. 11 and 12). The fluoroscopic examination of the diaphragm showed the motion of both sides of the diaphragm to be equal and normal.

A clinical diagnosis of a right subcostosternal diaphragmatic hernia was made and temporary interruption of right phrenic nerve followed by abdominal repair of hernia was done June 19, 1940.

Temporary interruption of the right phrenic nerve by crushing the nerve was done through a right supraclavicular incision. The abdomen was then explored through an abdominal right rectus incision under cyclopropane anesthesia. The ileocecal coil was found to extend over the left lobe of the liver and through an opening in the right anterior part of the diaphragm. There was also herniation of a portion of the omentum. These structures were moderately adherent but were removed without difficulty and were dropped back into the abdomen. After removal of the herniated viscera, the defect in the anterior right part of the diaphragm could be visualized. This opening was chiefly in the right side of the diaphragm but extended beneath the sternum. The portion of the opening to the right corresponded to the foramen of Morgagni. There also had been a lack of fixation of the diaphragm to the lower end of the sternum. The opening was about 6 centimeters in length along the costosternal attachment and it was about 4 centimeters in width. There was a complete hernial sac consisting of peritoneum of the diaphragm and anterior abdominal wall. This sac extended into the thoracic cavity for about 8 to 10 centimeters. The round ligament of the liver extended with the hernial sac into the thoracic cavity and the opening was to the left of the round ligament. The left lobe of the liver was very much smaller than normal and was rounded in contour. The right lobe was about normal in size and shape.

The hernial sac was removed from the thoracic cavity and partially excised, and the margins of the defect in the diaphragm were closed by overlapping and fixing the diaphragm to the chest wall with two sutures of continuous fascia lata removed from the right thigh. The round ligament, which had been cut from its attachment to the sac, was then incor-

Fig. 11.

Fig. 11. Case 3. Anteroposterior view on admission. Subcostosternal diaphragmatic hernia (foramen of Morgagni) with herniation of ileocecal coil into right side of thoracic cavity.

Fig. 13.

Fig. 12.

Fig. 12. Case 3. Lateral view on admission. Shows ileocecal coil herniated through an opening in anterior portion of diaphragm.

Fig. 13. Case 3. Five weeks after repair of hernia. Ileocecal coil in normal position in right lower quadrant of abdomen.

porated into the closure and fixed to the anterior chest wall. The fascia lata was fixed in the tissue with interrupted silk sutures. Although there was nonrotation of the cecum, it had a relatively long mesentery. The appendix was retrocecal and showed evidence of chronic inflammation; therefore, appendectomy was done. No attempt was made to fix the cecum in its normal position in the right lower quadrant of the abdomen. The abdomen was closed.

The patient was immediately placed in an oxygen tent where he remained until the third postoperative day. His postoperative course was without incident. He was dismissed from the hospital on the seventeenth postoperative day and from our care one week later. At that time the wound was entirely healed and he was feeling very well generally. The roentgenogram of the colon showed it to be in normal position with the cecum in the right lower quadrant of the abdomen (Fig. 13).

This patient presented the subjective symptoms to be expected in cases in which a part of the intestinal tract is involved in the hernia. These symptoms are those of intermittent intestinal obstruction. In this instance the obstruction was partial; however, this could become complete at any time. The most interesting consideration in this case is the portion of the intestinal tract which was involved in the hernia; namely, the cecum, appendix, ascending colon, and terminal ileum.

It is interesting to speculate at what time in life this hernia occurred. It was quite evident that there was nonrotation of the colon, as this portion of the bowel is very unlikely to herniate through the anterior portion of the diaphragm after the cecum has once attained its normal position in the right lower quadrant of the abdomen. The nonrotation of the colon would indicate that this hernia may be of congenital origin, although it is difficult to understand why the symptoms had not been present until about the patient's twentieth year of age if the nonrotated ileocecal coil had been in the hernia since birth. The possible congenital origin of this hernia is also suggested by the fact that the ileocecal coil, upon being released from the hernial opening, very soon attained its normal position in the right lower quadrant of the abdomen as shown by the roentgenogram of the colon taken 3 weeks after operation. That this normal position of the cecum was attained by the intestine although no attempt at mechanical fixation of it in this position was made at the time of operation indicates that the bowel had never had a previous opportunity to attain its normal position.



Fig 14, left Case 4 Anteroposterior view on admission Subcostosternal diaphragmatic hernia with herniation of large portion of transverse colon into right side of thorax

Fig 15 Case 4 Lateral view, on admission, shows that colon has herniated through an opening in anterior portion of diaphragm

**CASE 4** A man, aged 34 years, consulted the clinic on March 24, 1937, because of repeated attacks of gas and belching with severe pain in the chest. He stated that 2 years prior to his admission

he had had an attack of sharp pain in the right upper quadrant of the abdomen which lasted for 5 days, following which he had considerable gastric distress. Three months later he had a severe attack of gas and belching with severe pain in the chest and over the heart after he had eaten "hamburger" and drunk beer. He could not lie down and morphine was required for relief. One week later he had a similar attack. Since this attack he had to take something to make his food digest. His appetite was good. Immediately after meals and occasionally between meals he would have a sensation of rumbling and rolling of gas in his chest. During some of these attacks he had pain in the right epigastrium and near the right shoulder blade. This pain might occur with or without relation to meals. Recently even a glass of water would make the stomach feel full. Although the patient became nauseated after meals he had never vomited. There had been no history of injury.

On physical examination the patient was found to be well developed and well nourished. His weight was 160 pounds (72.6 kilograms). Examination of the abdomen revealed tenderness in the epigastrium and right lower quadrant. The blood pressure was 124 milligrams of mercury systolic and 80 diastolic. The results of urinalysis were negative. The hemoglobin was 18.5 grams per 100 cubic centimeters of blood, erythrocytes numbered 4,970,000 and leucocytes 11,500 in each cubic millimeter of blood. The flocculation reaction was negative.

Röntgenograms of the chest revealed a circumscribed shadow in the right cardiophrenic angle above the right side of the diaphragm. A diaphragmatic hernia was suspected. The roentgenogram of the stomach showed it to be in normal position. The roentgenogram of the colon revealed

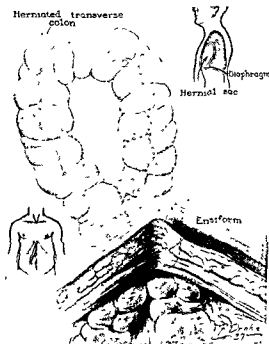


Fig 16 Case 4 Entire transverse colon and omentum herniated through a large subcostosternal opening (foramen of Morgagni), right of midline.



Fig. 17, left. Case 4. On dismissal. Colon in normal position below diaphragm.

Fig. 18. Case 4. One year after repair of subcostosternal hernia. Pleuritic adhesions right costophrenic angle. Lung fields negative.

herniation of a large portion of the transverse colon into the right side of the thoracic cavity, through an opening in the anterior part of the diaphragm (Figs. 14 and 15). The colon extended to the level of the second rib anteriorly. A diagnosis of subcostosternal diaphragmatic hernia with herniation of the transverse colon into the right side of the thoracic cavity was made.

Operation was performed on March 31, 1937, under cyclopropane anesthesia through an upper right rectus abdominal approach. On exploration of the abdomen it was found that the omentum and entire transverse colon had herniated through an opening in the anterior part of the diaphragm which was beneath the sternum, extending mostly to the right side but partly to the left side of the sternum. The opening measured about 10 centimeters in diameter and extended across the entire anterior portion of the chest wall. The colon and omentum were moderately adherent to the peritoneal sac which extended to the second rib anteriorly in the right side of the thoracic cavity (Figs. 16 and 19).

After removal of the colon and the omentum from the opening, it was found that there was a complete hernial sac of peritoneum which was a continuation of the peritoneum of the diaphragm and anterior abdominal wall. After removal of the herniated abdominal viscera, there was marked suction through the hernial opening, but this was due to the suction of air into the hernial sac as there was no direct communication with the pleural cavity. The round ligament of the liver was incorporated in the portion which formed the hernial sac and extended into the thoracic cavity. Both the round and falciform ligaments were pulled out of the thoracic cavity, but it was impossible to remove the hernial sac because of its firm attachment to the thoracic viscera and chest wall, high in the thoracic cavity. The round ligament of the liver was cut and the end distal to the liver, which had been attached to the abdominal wall, was permitted to retract into the thorax with the hernial sac (Figs.

20 and 21, frontispiece). Linear incisions were made into the sac to permit fluid to drain out after closure of neck of hernial sac. The opening was closed by suturing it to the posterior sheath of the rectus muscle on both sides. The tissues were first stabilized with silk, and then living sutures of fascia lata,

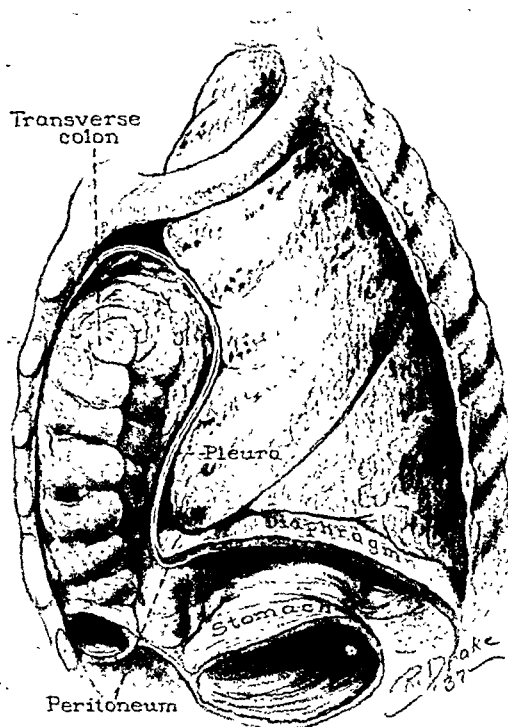


Fig. 19. Case 4. Hernial sac of peritoneum and pleura, anterior right portion of thorax, containing herniated transverse colon and omentum, compressing right lung.



Fig 14, left Case 4 Anteroposterior view on admission Subcostal diaphragmatic hernia with herniation of large portion of transverse colon into right side of thorax.

Fig 15 Case 4 Lateral view, on admission, shows that colon has herniated through an opening in anterior portion of diaphragm

**CASE 4** A man, aged 34 years, consulted the clinic on March 24, 1937, because of repeated attacks of gas and belching with severe pain in the chest. He stated that 2 years prior to his admission

he had had an attack of sharp pain in the right upper quadrant of the abdomen which lasted for 5 days, following which he had considerable gastric distress. Three months later he had a severe attack of gas and belching with severe pain in the chest and over the heart after he had eaten "hamburger" and drunk beer. He could not lie down and morphine was required for relief. One week later he had a similar attack. Since this attack he had to take something to make his food digest. His appetite was good. Immediately after meals and occasionally between meals he would have a sensation of rumbling and rolling of gas in his chest. During some of these attacks he had pain in the right epigastrium and near the right shoulder blade. This pain might occur with or without relation to meals. Recently even a glass of water would make the stomach feel full. Although the patient became nauseated after meals he had never vomited. There had been no history of injury.

On physical examination the patient was found to be well developed and well nourished. His weight was 160 pounds (72.6 kilograms). Examination of the abdomen revealed tenderness in the epigastrium and right lower quadrant. The blood pressure was 124 milligrams of mercury systolic and 80 diastolic. The results of urinalysis were negative. The hemoglobin was 18.5 grams per 100 cubic centimeters of blood, erythrocytes numbered 4,970,000 and leucocytes 17,500 in each cubic millimeter of blood. The flocculation reaction was negative.

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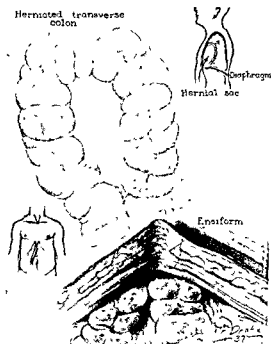


Fig 16 Case 4 Entire transverse colon and omentum herniated through a large subcostal opening (foramen of Morgagni), right of midline

# CEREBRAL ARTERIOVENOUS ANEURYSMS

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**D**IRECT communication between the arterial and venous systems of the body exists either as an acquired lesion due to trauma or disease, or as a developmental anomaly. Abnormal communications between intracranial vessels external to the brain occur chiefly between the internal carotid artery and the cavernous sinus. These extracerebral lesions arise spontaneously in diseased vessels or, as more frequently happens, they result from trauma. Their formation is dependent upon an anatomical arrangement that has no analogy elsewhere in the body. But abnormal communications between the pial and cerebral arteries and veins are probably always congenital, and it is this latter type of lesion with which the present study is concerned.

The arteriovenous communications of the brain in the past have been variously designated. Cushing and Bailey (3) in their monograph, *Tumors Arising from the Blood Vessels of the Brain* (1928), which was the first noteworthy attempt at clarification of the subject, referred to these lesions as angioma arteriole. They listed the following synonyms: angioma plexiforme or anastomoticum, varix arteriole or aneurysmaticus, Rankenangioma or Ranken-aneurysm, angioma varicosum or cirroides, and hemangioma racemosum arteriole et venosum. Synonyms used by others have been: angioma cavernosum, varix aneurysmaticus, aneurysma serpentina, aneurysm anastomatica. Dandy (1928) chose to call the lesions simply arteriovenous aneurysms. The latter term is perhaps the most useful, principally because it leaves no doubt about the nature of the lesion.

The reports of about 75 cases have accumulated in the literature, and there has been considerable variation and some misunderstanding in regard to the nature of the lesion, the interpretation of its clinical manifestations, and the possibilities for treatment. Personal

experience with a group of 6 cases having arteriovenous aneurysms of the brain in which careful investigations have been made and the progress observed after a variety of therapeutic measures, has prompted this reconsideration of the subject.

**CASE 1.** Frequent headaches since the age of 4, and infrequent convulsive seizures since the age of 26 in a 41 year old man. Slight increase in intracranial pressure and calcified areas in the left frontal lobe. Cephalic bruit, not discovered before operation. Distortion of the ventricles seen by ventriculography. Arteriovenous aneurysm of the left frontoparietal area of brain disclosed by osteoplastic operation. Subtemporal decompression. Improvement in headaches and convulsions 4 years later.

On July 24, 1936, Frank B., aged 41, a plasterer, referred by Dr. Edward M. Livingston of New York City, was admitted to the hospital, complaining of headaches and convulsive seizures.

At the age of 4 years the patient was critically ill in Italy with what was thought to be typhoid fever. After recovery from this illness he began shortly to experience periodic headaches which occurred every 3 to 4 weeks. These headaches were dull and usually bifrontal, occasionally associated with vomiting, and lasted on an average of 8 hours. They continued to recur through the years and, although he was sometimes confined to bed with them, he usually found sufficient relief from aspirin to continue his activities.

Three years before admission a new type of headache replaced the old one. This headache appeared almost daily and events associated with it followed a definite pattern. He would first experience a "burning sensation in the pit of the stomach" followed within a few minutes by a pain in the left supraclavicular region which, within the next 10 to 20 minutes, gradually traveled up the left side of his neck to the face, then "swept over the left side of the head" and centered in the left forehead as a violent throbbing pain. This would be associated with a watering of the left eye and temporary haziness in the vision of that eye. Ten grains of aspirin taken with the onset of the pain would give him relief within 20 to 30 minutes. He was unable to relate the onset of these headaches to any known incident.

He had his first convulsive seizure at the age of 26 (15 years before admission), and had about 1 a year thereafter. Three attacks occurred at night while he was asleep and one occurred while he was sitting quietly; all the others occurred during the activity of his waking hours. With the onset of an attack he felt a "quivering in the stomach" (unlike the sensation preceding headache) and this was followed by

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an uncontrolled cry and loss of consciousness. The attacks were always generalized according to the account given and lasted 20 to 40 minutes. There was no relationship between headaches and the convulsions, and at the termination of a convulsion he felt only extreme fatigue and had no local paresthesias or paresthesias.

His general physical condition was not remarkable: his intelligence and mental attributes were above average. There were no nevi or abnormal pigmentations over the body. The blood pressure was 118/70, the cardiac rate was 70 and the radial pulse was of normal character. There were a few prominent pulsating vessels in the left frontotemporal region, but the great vessels of the neck were not abnormally pulsatile and no bruit was discovered over the head or neck prior to operation. There was a definite bilateral papilledema of less than one diopter, greater on the left. The retinal vessels, both arteries and veins, were full and tortuous and difficult to distinguish from each other. Visual fields and acuity were normal. Quantitative smell function on the left was one third that on the right. Other functions of the head were normal as were motility and sensory functions and reflexes over the body.

Blood and urine tests were normal. The spinal fluid was under moderate increase in pressure (220 mm of water) and the total protein was 0.50 grams per cent.

Roentgenograms of the head showed the cranium to be of normal size, shape, and thickness. The frontal sinuses were of medium and equal size. There was very slight accentuation of the convolutional markings of the skull, and the posterior clinoid processes were atrophic. One or two local areas of rarefaction appeared to be the result possibly of pressure from the vessels of the aneurysm. The vascular markings (diploe) were accentuated, particularly on the left in front and near the vertex. There was increase in the size of the groove for the middle meningeal artery on the left as compared to the right, the foramen spinosum was not well demonstrated. The pineal was calcified and in normal position. There was spotty calcification in left frontoparietal region at a site corresponding to precentral area of cortex. There was also calcification in intracranial segment of left internal carotid artery.

A diagnosis of tumor, probably meningioma, of the left frontal cerebral lobe was presumed.

Ventriculography was performed, July 27, 1936. Thirty cubic centimeters of clear fluid, found under moderate increase in pressure, were exchanged for air. The roentgenograms showed normal sized ventricles, but a slight shift of the lateral and third ventricles to the right and a slight depression of the left frontal horn (figs. 1a and b).

Operation was done July 30, 1936. After ether anesthesia had been administered, a left parietal osteoplastic operation was performed (fig. 2). Neither the scalp nor the bone appeared unduly vascular but upon elevation of the bone from the dura, enlarged and tortuous middle meningeal ar-

teries tore easily and bled briskly. As the dura was reflected from the brain, large tortuous and intertwined vessels were revealed in the upper part of the prerolandic area. These vessels were obviously large veins but were tense, pulsating, and had an arterial color. They appeared to extend on up to the sagittal sinus and downward into the lateral cerebral fissure but in this latter direction they were smaller. Elsewhere over the exposed frontal lobe all cortical vessels were several times larger than normal and even those that could be distinguished as veins had a red dish arterial color. In addition, there were several stubby vessels, 2 to 3 millimeters in diameter, connecting these cortical vessels and the dural arteries. No attempt was made to ligate any of the vessels except those communicating with the dura. A fair sized decompression was created beneath the temporal muscle and the bone flap was replaced and sutured.

The recovery from operation was prompt and the only complication was a transitory aphasia which disappeared by the twelfth postoperative day. The headaches were greatly improved. A bruit was heard faintly on auscultation over the left parietal area near the midline and could easily be overlooked if it were not anticipated. The bruit was quite distinct over the area of decompression but it was not heard elsewhere over the head. It was faintly heard over the left eyeball and left carotid artery in the neck. The patient was not aware of noises in the head at any time. Compression of the left common carotid artery caused slight diminution in the bruit; of both carotids, almost complete obliteration of the bruit.

After operation, 1050 r units of roentgenotherapy were administered in 10 doses. The decompression though slightly full was not tense. There was no essential change in the appearance of the optic fundi.

The patient was seen at regular intervals in the 4 years after operation. Two additional series of roentgenotherapy, each of 1,000 r units, were given during first 6 months but patient refused more.

He was greatly relieved of his headaches for a year after operation. After that he again began to have daily left frontal headaches but of much less severity than before operation. These headaches were unaccompanied by the former pain in the left shoulder, neck, and face. He took no medication except aspirin and had but one mild convulsion (September, 1938).

No new physical signs developed. The bruit remained the same. The decompression varied in its fullness but the optic disks remained slightly full.

Headache was the complaint that finally brought this patient to the hospital. It had first appeared at the age of 4 years and is fairly good evidence that his vascular lesion was present early in life. The headache of later years had many of the aspects of migraine by its involvement of one side of the neck, face, and head, at least it was characteristic of pain of vascular origin. Since the large

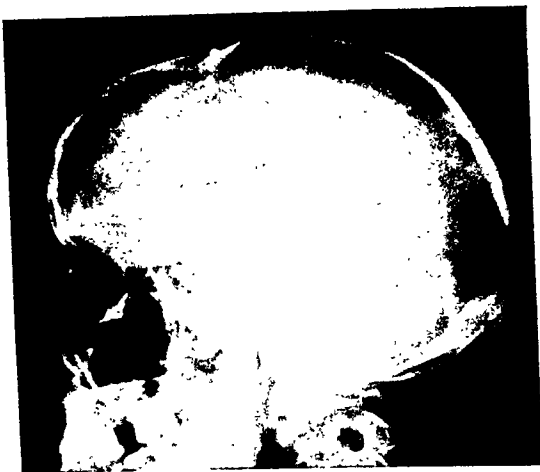


Fig. 1a. Case 1. Ventriculogram showing deformity of the body and frontal horn of the left lateral ventricle.

cerebral vessels were the most conspicuous feature of this man's lesion it might be supposed that dilatation of these vessels was directly responsible for at least the pain in the head, but since the normal pial vessels over the cerebral convexity are not pain sensitive this explanation is improbable (20). A more reasonable explanation for the headache would be the distention of the pain sensitive dural arteries which in this individual were seen not only to be enlarged but also in direct communication with the large vessels of the aneurysm. Transection of the middle meningeal artery low in the temporal region interrupted both the proximal blood supply and the nerve supply to the distal portions of that artery. This alone is sufficient to cause improvement in headache (9). The partial return of headache a year or so later might well result from return of nerve supply to the dural arteries.

Slightly increased intracranial pressure was evidenced by the low grade papilledema. In all probability there had been fluctuations of intracranial pressure in the past. The lack of fullness of the decompression except for the first several days after operation demonstrated the absence of marked or sustained elevation of pressure. The decompression and the interruption of the middle meningeal artery doubtless each deserve some of the credit for the improvement in patient's headaches and the diminution in the frequency of convulsions.

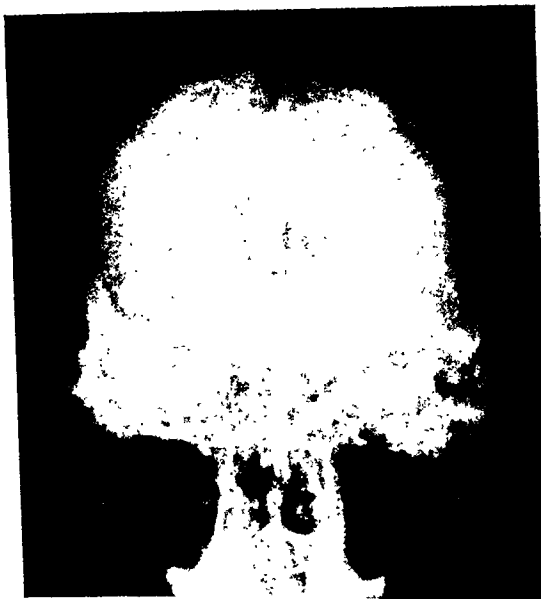


Fig. 1b. Case 1. Ventriculogram showing depression of the lateral ventricle on the left side.

CASE 2. Occasional paresthesias and convulsive movements in left upper extremity for 3 years and mild schizoid psychosis for 6 months in woman, aged 43. Arterial hypertension and slight left hemiparesis. Cephalic bruit, not discovered before operation. Distortion of the ventricles seen by ventriculography. Arteriovenous aneurysm of right parietal area of brain disclosed by osteoplastic exploration. Subtemporal decompression. Roentgenotherapy. Diminution in frequency and severity of convulsions but increase in psychosis 4 years later.

On September 1, 1936, Helen R., aged 43, an unmarried grade school teacher, referred by the Rockefeller Institute and the Payne Whitney Psychiatric Clinic of New York City was admitted to hospital, complaining of attacks of numbness and weakness in the left hand and arm.

Until 3 years before admission she had been in good health and without complaint. At the age of 40 she began to experience periodic sensations of a "numb, cold, dead feeling" in the left hand and arm which sometimes spread over the entire left side of the body. The attacks occurred at first about once a month but later as often as several times a week and lasted from 1 to 15 minutes. At the age of 41 the attacks of paresthesia became associated sometimes with an uncontrolled tonic contraction of the left hand and arm. During the year before admission to the hospital she lost consciousness several times in the course of these attacks but never had a generalized convulsion.

A typical attack was ushered in usually by a sensation of pounding in her ears, a "rushing of blood to the head" and a "beating sensation all over the



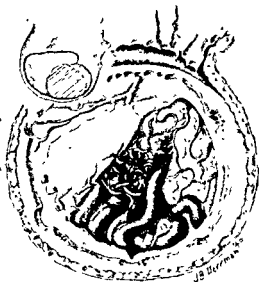


Fig 2 Case 2 Drawing made from postoperative sketch giving site and general appearance of the lesion. Note abnormal vessels anastomosing the lesion and the middle meningeal artery.

body." She had no tinnitus between attacks and never had headache at any time.

A year prior to admission she was found to have unexplained hypertension. Examination showed slight enlargement of the heart to the left and electrocardiographic changes indicating left ventricular preponderance, but no renal pathology.

During the 6 months prior to admission she developed distinct changes in mood, was overly suspicious of people, and had hallucinations of hearing voices. A sister had committed suicide during a state of depression. After the patient had been observed at the psychiatric clinic, a diagnosis was made of "paranoid reaction with panic episodes", the prognosis was thought to be serious. It was while she was being observed in this clinic that a left sided convulsive seizure was seen by a physician for first time.

Examination disclosed no papilledema but the vessels of the right retina were full and tortuous, the veins were of a lighter color than usual. Visual acuity and perimetry were normal. There was very slight weakness of the left lower face and of the left upper extremity. There were no sensory changes. The deep reflexes in the left upper and lower extremities were increased but the superficial reflexes were normal. The blood pressure at rest averaged 165/108 and the cardiac rate averaged 80. The pulse had a bounding quality. The heart was normal on physical examination although it was shown to be slightly enlarged to the left by roentgenography.

Laboratory studies of the blood and urine showed normal values.

Roentgenograms of the head (Figs. 3a and b) showed the cranium to be of normal size, shape, and thickness. The frontal sinuses were of moderate and equal size. There was very slight accentuation of the convolutional markings of the skull and the posterior clinoid processes were thin but there was no frank evidence of increased intracranial pressure. There were one or two areas of rarefaction of the inner table of the right parietal bone, possibly the imprint of vessels of the aneurysm. The vascular markings (diploe) were accentuated over the entire skull and in the parietal regions there were the markings of large venous lakes. The groove for the right middle meningeal artery was increased in size although there was no change in the size of the foramen spinosum. There were no intracranial calcifications except in the falx cerebri.

A diagnosis of right frontoparietal neoplasm was presumed.

Ventriculography was carried out on September 1, 1936. The ventricular fluid was found to be clear and under slightly increased tension. Twenty cubic centimeters of fluid were removed and exchanged for air. Roentgenograms showed normal sized ventricles with no lateral shift, but the superior wall of the body of the right lateral ventricle had a serrated appearance as from the projection of nodular lesions into the ventricle.

Operation was performed September 1, 1936. After ether anesthesia had been administered, a right parietal osteoplastic operation was performed. Neither the scalp nor the bone was unduly vascular, and the dura was not adherent to the bone. The middle meningeal artery, however, was about twice the expected size and bled vigorously when cut. When the dura was reflected a number of tortuous vessels, some as large around as a lead pencil or larger, were seen to overlie the precentral area almost completely obscuring the cortex. Tense and tortuous vessels of smaller caliber and less closely arranged were present over the rest of the exposed area. Bright red blood was seen swirling through the larger vessels and a thrill was felt on palpating them. There were no normal looking arteries or veins in the exposed field. Three short but wide vessels passed directly from one of the cortical vessels to the dura and were seen to anastomose with dural arteries; these were clipped and cut. A fairly large subtemporal decompression was made and wound closed.

Recovery from operation was uncomplicated. The bruit, which had not been discovered before operation, was distinct but of low intensity over the right frontoparietal region over the right eyeball, and over the right carotid artery in the neck. The patient herself was never aware of the bruit even when it was suggested that she might hear it. Compression of the right carotid artery diminished the intensity of the bruit about half. The decompression was never found to be tense during the recovery period. Roentgenotherapy totaling 1100 r units was administered within 2 weeks after operation had been performed.



Fig. 3a. Case 2. Lateral roentgenogram of the skull showing accentuation of the diploic channels.

Repeated series of roentgenotherapy were administered over the next 18 months until a total of 10,200 r units had been given. The patient had rare attacks of uncontrolled clonic contractions in the left upper extremity in the 4 years after operation. There was no advance in her signs but the bruit seemingly became less loud. The blood pressure remained the same. Her paranoid trend and the hallucinations of voices became progressively evident, and she was placed in an institution.

The combination of focal convulsive seizures and marked increase in the vascular markings of the skull should have suggested the possibility of a cerebral arteriovenous aneurysm. Had a bruit been listened for over the head the diagnosis could have been made before operation. Even so, an exploratory operation would have been justified because meningiomas, which these lesions are likely to resemble in their clinical manifestations, sometimes possess a bruit and comparable vascularity of the skull. The decompression and the roentgenotherapy, one or both, seem to have afforded some benefit, for the convulsive attacks have been much less severe and less frequent. The possible causative relation of the cerebral lesion to the psychosis is purely speculative. The several psychiatrists who examined the patient were about equally divided on the question.

CASE 3. Recurring convulsions since the age of 14 in a boy 20 years old. Cephalic bruit. Distortion

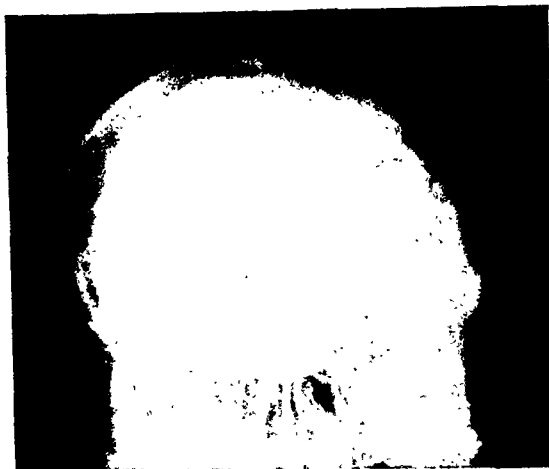


Fig. 3b. Case 2. Posteroanterior roentgenogram of the skull showing accentuation of diploic channels.

of ventricles seen by ventriculography. Arteriovenous aneurysm of right frontoparietal area of brain disclosed by osteoplastic exploration. Subtemporal decompression. Maximum roentgenotherapy. Ligation of right common and external carotid arteries. Cerebral angiography. Ligation of left internal and external carotid arteries. Marked diminution in cephalic bruit and cessation of grand mal convulsions one year after last operation.

First admission to the hospital October 6, 1936. Mike B., aged 20 years, an electrician's helper, complained of recurring convulsive seizures which had been present since the age of 14.

The patient's birth had been unremarkable and he had had no notable illnesses or injuries. At the age of 14 he began to have convulsions which recurred about every 3 months at first, but gradually increased in frequency until they averaged one a week. About one-fourth of the attacks occurred at night. The attacks were all generalized and associated with loss of consciousness but sometimes there were short prodromal symptoms in the left arm. Regular doses of phenobarbital failed to diminish the attacks.

Examination revealed his general physical condition not remarkable and his intelligence average. Prominent, pulsating vessels were present over the right frontotemporal area and in the midforehead. The blood pressure averaged 110/66 on each side, the cardiac rate was 75, and there was a faint systolic murmur at the apex. A bruit synchronous with the pulse was audible, over the right frontal and parietal regions of the head and over both eyeballs. There was no increased pulsation of the vessels of the neck but there was a bruit over those on the right. Compression of the right carotid artery diminished the bruit; compression of the left caused no change. The bruit was not audible to the patient. The optic



Fig 4a Case 3 Lateral roentgenogram of the skull showing rarefied areas in the right frontoparietal region resulting from direct pressure of the vessels of the aneurysm



Fig 4b Case 3 Roentgenogram of the base of the skull showing enlargement of the right foramen spinosum

fundi were normal in appearance. The motility functions, sensation, and reflexes were normal.

Blood and urine tests were normal. The spinal fluid was under slight increase in pressure (200 mm of water). Roentgenographic studies of the heart and the electrocardiogram were normal.

Roentgenograms of the head (Figs 4a and b) showed the cranium to be of normal size, shape, and thickness. The frontal sinuses were large and equal. There was very slight accentuation of the convolutional markings of the skull and slight thinning of the posterior clinoids but no frank evidence of increased intracranial pressure. There were several areas of rarefaction of the inner table of the right parietal bone, the result of erosion from large, pulsating vessels of the aneurysm. The vascular markings (diploe) were moderately accentuated on both sides. The grooves for the middle meningeal arteries were accentuated on both sides but more so on the right and the foramen spinosum on the right was twice the size of that on the left. There were no intracranial calcifications.

Pneumoencephalography was carried out October 7, 1936. One hundred and twenty cubic centimeters of fluid were removed and an equal amount of air was injected without producing any noteworthy change in the patient's condition. Roentgenograms showed the ventricles to be of normal size, but the body and frontal horn of the right lateral ventricle were depressed and the entire ventricular system was displaced slightly to the left. The markings of sulci over right hemisphere were distorted.

A diagnosis of arteriovenous aneurysm of the right parietal region was made.

Operation was performed October 10, 1936. After ether anesthesia had been administered, a right parietal osteoplastic flap was made. The vascular-

ity of the scalp was somewhat increased and the bone bled freely from the cancellous portion; one diploetic vein actually spurted blood. The dura was not adherent to the bone but the middle meningeal artery was large and thicker walled than usual and the groove it had caused in the skull was deep. Several rounded bluish humps of the dural surface gave clues to the presence of large cortical vessels beneath. Rounded erosions in the skull were the imprints from the pressure of these vessels. The dura was reflected from the brain revealing a mass of tortuous, sometimes intertwining and overlapping vessels, some of which measured a centimeter or more in diameter. They partly overlay the motor cortex but were chiefly anterior to it and appeared to continue on beyond the exposure, anteriorly and superiorly. The vessels all had a reddish color, some were thin walled and arterial blood was seen streaming through them with each pulsation. A faint thrill was detected upon palpation of the vessels. In a number of places the dura was adherent to the pia-arachnoid by either flimsy or tough fibrous bands and at other places short vessels, 1 to 2 millimeters in diameter, passed directly from the cortical vessels to the dura. No attempt was made to ligate any of the cortical vessels but the dura was freed all around and the vascular attachments were transected. A fair sized subtemporal decompression was created before the flap was replaced and sutured.

Recovery from the operation was prompt and uneventful but for a convulsion 10 days after operation which, for the first time, was followed by a left hemiparesis that did not clear up for several days. Roentgenotherapy directed to right parietal region of the head was started before he left the hospital.

For the next 28 months he came regularly for roentgenotherapy and received 600 r units to each

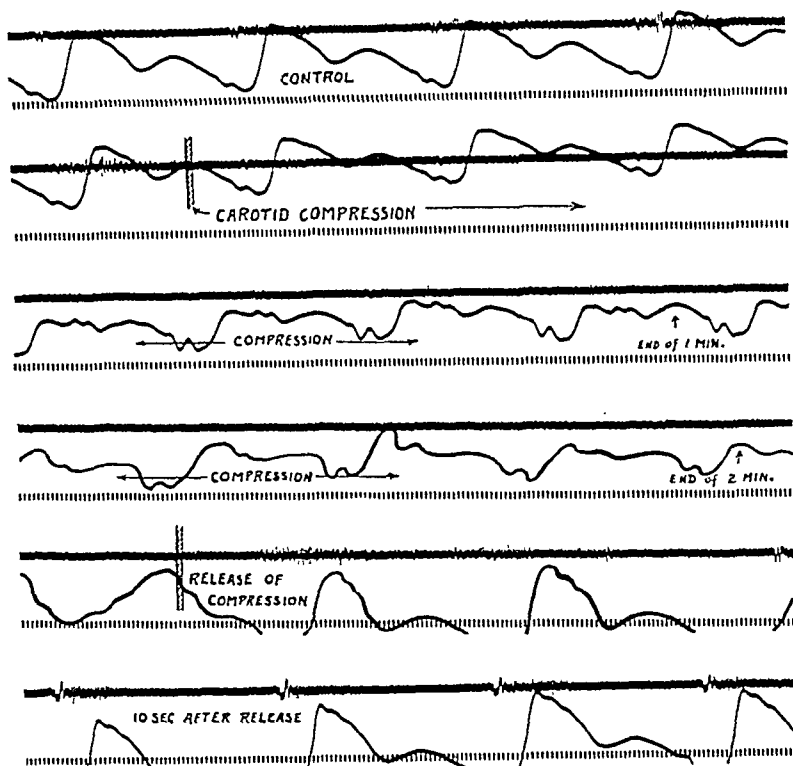


Fig. 5. Case 3. Stethographic record of cephalic bruit and simultaneous pulse record showing marked diminution in bruit with compression of the left common carotid artery.

of two parietal ports with each series. The series was repeated about every 8 weeks until he had received a total dosage of 13,200 r units. This resulted in complete and permanent alopecia of the scalp in the right parietotemporal region and comprised the limit of possibilities with irradiation. Although the major attacks were less frequent during this period after operation, petit mal seizures occurred on an average of every week; the latter were characterized by turning the head to the left and strongly flexing the left upper extremity. The decompression sometimes appeared full but never tense except just after a major convulsion.

*Second admission:* to the hospital March 15, 1939. Because of the lack of material change in the number of convulsive seizures, although the proportion of major seizures had lessened, and because the maximum of roentgenotherapy had been given, he was readmitted for further operative procedure.

Although the irradiation had caused alopecia, some atrophic changes and telangiectasis of the scalp, there were in the region several tortuous and pulsating superficial vessels which obviously had not become thrombosed as a result of the therapy. The decompression was flat. The bruit was the same as it had been originally but its intensity was greatly

diminished by compression of the right common carotid artery. A stethographic record of the bruit with and without compression of the carotid showed this diminution. Since repeated and prolonged compression of the carotid produced no untoward effects, ligation of the vessels in the neck was decided upon.

Operation was done March 23, 1939. Occlusion of the right common carotid artery was accomplished by ligation with autogenous fascia lata and of the right external carotid artery by wrapping it with double silk. The arteries were estimated to be about twice normal size when first exposed, and there was a palpable thrill over them.

*Postoperative and subsequent course.* Recovery from operation was uncomplicated, and no signs of palsy developed. There was no material change in the blood pressure or pulse. The bruit over the head became faint and was indistinct over the right eyeball; over the left globe it remained the same. For the next 7 months the intensity of the cranial bruit increased somewhat but was less than its original intensity. The convulsions changed neither in quality nor frequency and after a series of 6 successive major attacks he was readmitted to the hospital. The use of sodium diphenyl hydantoinate for 3 months did not alter the convulsive seizures.

*Third admission* to the hospital was November 13, 1939. Because of continuation of convulsions without material improvement after subtemporal decompression, maximum roentgenotherapy, and occlusion of the right common and external carotid arteries, he was admitted for restudy and, possibly, further operation.

Examination showed no essential changes from those recorded heretofore except that vessels of the scalp had become more prominent on the left side since the ligation of the right carotid arteries. There was no change in motility function, sensation, or reflexes. The decompression was slightly full but soft and pulsated freely. The bruit was readily heard over the decompressed area but faintly over the right frontal area and over the right eyeball, it was loudest over the left eyeball and of moderate intensity over the left carotid. The blood pressure remained at an average of 110/80 and the cardiac findings were normal.

Electroencephalography was carried out by Dr. D. J. Simon. A summary of the findings showed abnormal cortical function over both cerebral hemispheres. The abnormality appeared greatest in frontal areas and was approximately equal on the two sides.

Compression of the left common carotid artery caused the bruit to disappear completely during the first 10 seconds. Thereafter a soft, low pitched bruit appeared and remained so during 5 minutes of compression. Compression of the artery for this length of time caused no loss of consciousness or special symptoms other than a full feeling in the head which was probably due to the simultaneous compression of the left internal jugular vein.

A stethographic record (Fig. 5) of the cranial bruit was taken before, during, and after 2 minutes of continuous occlusion of the left common carotid artery. This record showed the disappearance of the major part of the bruit. It was interesting to find that with this sensitive machine, by which intensity and frequency of sound could be recorded, there was relatively greater change following occlusion of the carotid than one might have guessed by merely listening with an ordinary stethoscope.

It was postulated that since the patient was still young and no untoward reaction followed 5 minute occlusion of the remaining common carotid artery, ligation of the artery would be comparatively safe and possibly beneficial.

Cerebral angiography was carried out November 24, 1939, after the injection of 20 cubic centimeters of thorium dioxide solution into the left common carotid artery. With the use of local anesthesia the left common carotid artery was exposed through a small incision. Just below the bifurcation of the artery the material was rapidly injected and roentgenograms were taken 4, 10, and 16 seconds after the injection was started.

The first roentgenogram (Fig. 6) showed the material crossing the anterior communicating artery and outlining the vessels of the aneurysmal lesion on the right side. None of the cerebral vessels on the

left side or elsewhere were visualized. On the second and third plates there was no evidence of the material remaining.

Immediately following the angiography, November 24, 1939, the patient was returned to the operating room and after local injection of procaine anesthesia the carotid arteries on the left were more widely exposed. The common and internal carotids were estimated to be about half again their normal size, and there was a faint thrill palpable over them. With traction and manipulation of the common carotid, the blood pressure suddenly rose to 200/120 and the pulse to 140 but they promptly returned to normal when the manipulations were discontinued. There was no recurrence of the phenomenon after injection of procaine into the carotid plexus at the bifurcation. A temporary ligature was placed upon the internal carotid and the patient was observed for 30 minutes. Since no untoward symptoms or signs developed, an occluding aluminum band was placed on the internal carotid artery just above the bifurcation.

Samples of blood were taken from the left internal jugular vein before and again 10 minutes after occlusion of the left internal carotid. The oxygen and carbon dioxide contents of the blood were as follows:<sup>1</sup> Before ligation of the artery—oxygen content, 19.8 volumes per cent, carbon dioxide content, 51.8 volumes per cent. After ligation of the artery (10 minutes after)—oxygen content, 14.8 volumes per cent; carbon dioxide content, 55.4 volumes per cent.

There were no postoperative complications. One short left sided convulsion, without loss of consciousness, occurred 12 hours after operation but there were no aphasia, palsy, or other untoward developments. The cephalic bruit was very greatly diminished in intensity and remained so. The bruit over the left eyeball, however, was markedly accentuated after the ligation, and the superficial vessels of the left side of the scalp became more prominent.

Operation again was performed December 7, 1939. After local procaine anesthesia, the 12 day old wound in the neck was reopened. A temporary ligature was placed upon the left external carotid artery and the patient observed for 20 minutes. Since no untoward symptoms or signs developed the artery was occluded by wrapping it with silk just above the bifurcation of the common carotid. The superior thyroid artery which was larger than normal was also occluded with a silk ligature.

Samples of blood were taken from the left internal jugular vein before and again 10 minutes after occlusion of the left external carotid and superior thyroid arteries. The oxygen and carbon dioxide contents of the blood were as follows. Before ligation of the arteries—oxygen content, 15.7 volumes per cent, carbon dioxide content, 54.8 volumes per cent. After

<sup>1</sup>The normal range for oxygen and carbon dioxide content of the blood is as follows: Arterial blood—oxygen content, 15 to 21 volumes per cent; carbon dioxide content, 45 to 55 volumes per cent. Venous blood—oxygen content, 10 to 18 volumes per cent; carbon dioxide content, 50 to 60 volumes per cent. The figures represent weighted averages of several investigations (11).

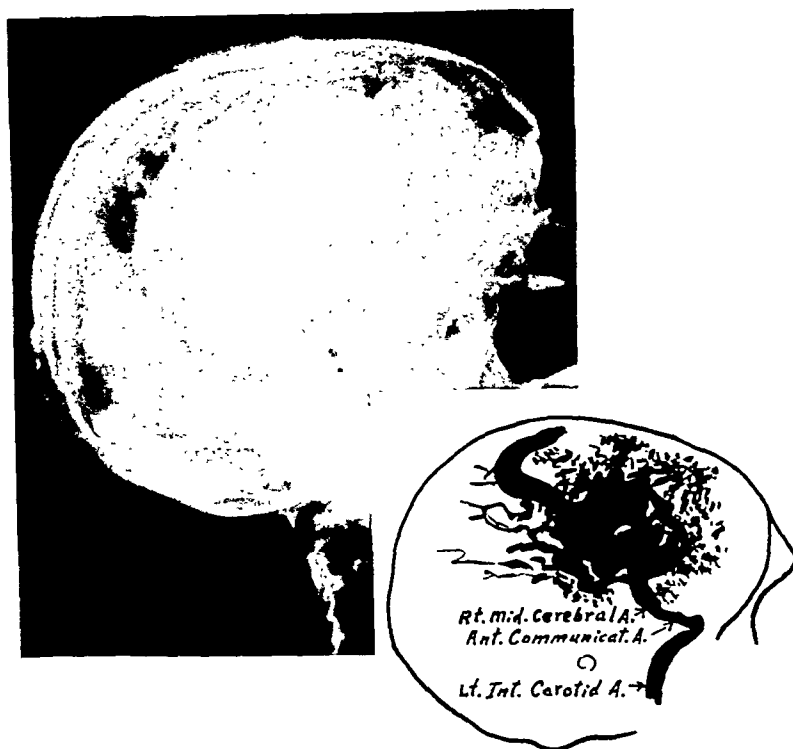


Fig. 6. Case 3. Cerebral angiography with injection of 20 cubic centimeters of thorotrast in the left common carotid artery. The substance has crossed to the right side and shows the large mid-cerebral artery feeding the "nest" of smaller vessels which connect with large veins near the sagittal sinus.

ligation of the arteries (10 minutes after)—oxygen content, 14.8 volumes per cent; carbon dioxide content, 57.1 volumes per cent.

Recovery from operation was uncomplicated. The intensity of the bruit over the left eyeball was materially diminished.

For several weeks after leaving the hospital he experienced momentary unsteadiness and blurring of vision on rising from a sitting or reclining position but this eventually ceased. In the year after operation he had no recurrence of grand mal convulsions. Attacks of uncontrolled, momentary turning of the head to the right without loss of consciousness occurred on an average of once a week. Paresthesias without convulsive movements or loss of power occurred in the left upper and lower extremities every 6 to 8 weeks. The bruit a year after operation was of low intensity over the left eyeball, almost undiscernible over the right eyeball, and very faint on the right temporoparietal region of the head. There were no visual or auditory disturbances, no palsies of the extremities, and no changes in sensation or in reflexes. He was taking .030 grams of phenobarbital three times daily, said he felt remarkably well, and was actively employed in a business of his own.

The close observation of this individual and the use of a succession of therapeutic measures over a period of 3 years have provided an abundance of information about cerebral arteriovenous aneurysms in general. It has been demonstrated that: The use of the maximum dosage of roentgenotherapy cannot be relied upon to affect the lesion, although it may well be that better results would have been obtained if the arterial ligations had been carried out first in order to diminish the blood flow through the lesion. Successive ligations of all the carotid arteries in both sides of the neck can be done, at least in some persons, with comparative safety. Doubtless youth and the extensive collateral circulation in the presence of the aneurysm makes this possible. There is extensive collateral circulation between the internal and external carotid systems, partly through the orbit. The effectiveness of diminishing the spill of arterial blood into the ve-

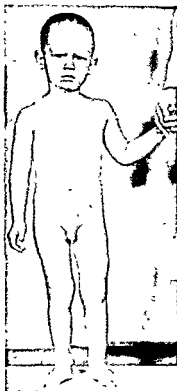


Fig. 7 Case 4 Photograph showing relative enlargement of the head

nous system by ligation of a carotid artery can be estimated by determining the oxygen and carbon dioxide content of the blood of the jugular vein before and after the ligation. The arterial anastomosis through the anterior communicating artery of the circle of Willis and the increase in the circulation time in the brain can be safely demonstrated by the injection of thorium dioxide into the carotid artery. Convulsions can be materially benefited by extensive occlusion of the carotid arteries.

The acute rise in pulse rate and blood pressure that occurred on manipulation of the carotid is an interesting phenomenon but has no special relation to the subject under discussion. It resulted, probably, from sudden decrease in the intrasinal pressure on occlusion of the common carotid artery. Similar experiences have been mentioned by others (8, 23).

**CASE 4** Two episodes of transient hemiparesis in a child of 2½ years. Large head, prominent vessels of the scalp and cephalic brist. Right cerebral arteriovenous aneurysm demonstrated by angiography and pneumoencephalography. Successive ligation of carotid arteries. Death following last ligation. Autopsy.

On December 13, 1938, George S., aged 2½, referred by Dr. Edgar Mayer of New York City, was admitted to the hospital with the complaint of attacks of transient left hemiparesis.

The child's birth was not remarkable and he was thought to be a bright and healthy boy until 2



Fig. 8 Case 4 Infrared photographs showing increased vascularity of the scalp

months before admission when he stumbled on a stairs and fell bumping his head. Not much was thought of this incident until 12 days later when it was noticed that his left foot was so weak he could hardly walk and within a short time thereafter the left arm hung limply. Over night he regained complete use of these extremities. A second and similar episode occurred 6 weeks later (1 week prior to admission).

On examination, the child was found to be happy, co-operative and, by Binet psychometric tests, to have "average intelligence and a fairly even level of function." The head appeared and measured larger in all dimensions than normal (Fig. 7). Veins of the scalp were unusually prominent and some pulsated (Fig. 8). On auscultation a bruit could be heard all over the head and over both eyeballs. Both a bruit and a thrill were present over large, briskly pulsating vessels in the neck. The retinal vessels were full and tortuous, particularly on the right, and the right pupil was larger. There was no exophthalmos or pulsation of the eyeballs. There was slight but definite left hemiparesis and increased deep reflexes on that side. The heart was enlarged and there was a systolic murmur heard all over the precordium. The blood pressure averaged 104/70 on both sides; the cardiac rate was 70 and the character of the pulses was suggestive of a "Corrigan pulse." Compression of either carotid in the neck diminished the intensity of the bruit, but compression of the right carotid produced the greater effect.

Laboratory tests on the blood and urine showed no abnormality. Spinal fluid examination showed questionable, slight increase in pressure but no other unusual findings; the total protein was .030 grams per cent and the cell count was normal. Electrocardiogram showed a slight left ventricular preponderance. Roentgenograms of the chest (Fig. 9a) showed moderate enlargement of the heart to the right and to the left, also moderate widening of the superior vena cava.



Fig. 9b. Case 4. Roentgenogram of the heart 4 weeks following ligation of the common and external carotid arteries on the side of the lesion. Note the diminution in the size of the heart as compared to the roentgenogram taken before operation (see Fig. 9a).

Roentgenograms of the head showed a thin skull and enlargement of the cranial vault. However, there was no widening of the sutures, or other signs suggesting increased intracranial pressure. The vascular markings of the skull (diploe) were slightly accentuated in frontal regions, more on the right. The groove for the right middle meningeal artery was larger than the left; no change in size of either foramen spinosum. There were no local areas of erosion in skull and no intracranial calcification.

Pneumoencephalography was done January 25, 1939. Ninety cubic centimeters of air were injected without producing any change in the patient's condition. Roentgenograms showed the left lateral ventricle to be larger than the right and the right one appeared slightly depressed; both were shifted slightly to the left. The sulcal markings over the right cortex had a curious mottled appearance.

Cerebral angiography was carried out, January 25, 1939, after the injection of 15 cubic centimeters of thorium dioxide solution into the right common carotid artery. After the administration of ether anesthesia the right common carotid artery was exposed through a short incision just below its bifurcation. Under vision, thorium dioxide was rapidly injected in 3 seconds and roentgenograms were taken immediately, while compression was kept on the proximal portion of the artery to diminish the flow of blood. A second plate was taken 7 seconds after the first and a third plate in another 7 seconds.

The first roentgenogram (Fig. 10) showed good filling of the right cerebral vessels and in the parietal region demonstrated many tortuous abnormal channels characteristic of an arteriovenous aneurysm. The second plate still showed faint shadows of the dispersed material but the third plate showed none.

Roentgenogram of the abdomen 5 days later showed the liver and spleen to cast dense shadows from the deposited thorium salt.



Fig. 9a. Case 4. Original roentgenogram of the heart showing general enlargement, more particularly to the right.





Fig 10 Case 4 Cerebral angiography by injection of 15 cubic centimeters of thorotrast in the right common carotid artery. Note the short course of the mid cerebral artery before it empties into the "nest" of smaller vessels which connect it with the larger veins near the sagittal sinus. The rolandic vein can be seen to be enlarged all along its course.



Fig 11 Case 4 Cerebral angiography by injection of 35 per cent diodrast in the left common carotid artery. Note the outline of normal vessels on the left side of the brain and the partial outline of abnormal vessels of the right frontal lobe. The dye has crossed through the anterior communicating artery. Note that a more anterior portion of the vascular lesion is outlined than in Figure 10.

Operation was performed February 15, 1939. After ether anesthesia had been administered, occlusion of the right common carotid artery was accomplished with a ligature of autogenous fascia lata and of the right external carotid artery with a ligature of double silk. These arteries were larger than would be expected in a normal child of this age. The internal jugular vein also was large and pulsated.



Fig 12 Case 4 Photograph of right side of the brain showing extensive distribution of the vascular lesion over the entire right frontal lobe as far back as the rolandic fissure.

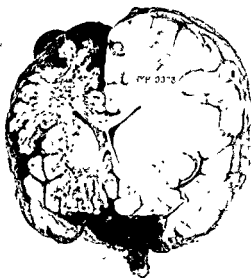


Fig 13 Case 4 Coronal section of the brain passing through the tips of the temporal lobes. The entire right hemisphere has a shrunken appearance which is the result both of the collapse of the numerous blood vessels and of the atrophy of the parenchyma. Many abnormal vessels are apparent on the surface, in the sulci, and in the substance of the hemisphere.



Fig. 14a. Case 4. A section through the cerebral cortex shows the walls of three adjacent vessels. One is a relatively thin walled artery *A*, and the 2 others are veins. One vein has an unusually thin wall, *B*, while the other has a thin wall on one side, *C*<sub>1</sub>, and a greatly fibrosed and thickened wall on the other, *C*<sub>2</sub>. There is phagocytic infiltration and softening of the brain, *D*, adjacent to the vein. (Masson stain,  $\times 45$ .)

There was no immediate untoward reaction as a result of the operation. The intensity of the bruit over the head was only slightly diminished although that heard over the right eyeball was now about one-fourth that over the left. There was no material change in the blood pressure or pulse but a roentgenogram of the heart (Fig. 9b) 4 weeks after the ligation showed a distinct diminution in the cardiac shadow, principally on the right side. On the second day after the ligation there suddenly developed marked weakness of the left side of the body. Since it came so long after the arterial occlusion, its occurrence was considered fortuitous and there was thought to be no reason for removing the ligatures. The weakness gradually disappeared over the next 10 days but suddenly recurred at the end of this period. This time a lumbar puncture was performed with the idea of demonstrating bloody spinal fluid, since these recurring palsies were thought to be due to successive hemorrhages; but the fluid contained no blood, no increase in white cells, or change in its protein content.

During the first 12 months after operation there were two additional episodes of transient left hemiplegia; like the others they came on rather rapidly over a period of several minutes during which time the child did not complain, had no convulsive movements, and did not lose consciousness. Recovery from each succeeding attack was less complete so that there developed considerable restriction in motion of the left extremities and he walked with a

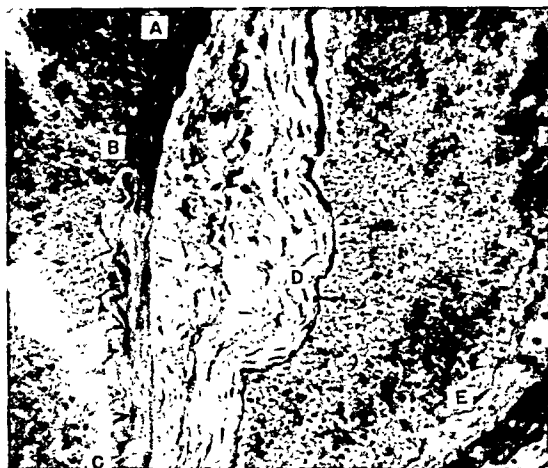


Fig. 14b. Case 4. Enlargement of area outlined in Fig. 14a. There is a region in the circumference of the artery (*A* to *B*) which is without elastica interna; elsewhere (*B* to *C*) there is a well developed elastica interna. Segments of the opposed walls of a single vein show the great fibrosis and thickening of one side (*D*), and the relatively thin wall of the other side (*E*). (Masson stain,  $\times 68$ .)

spastic gait. The vascularity of the scalp did not diminish from its original state nor did the bruit over the head change, although it was much less distinct over the right eyeball.

In February and March, 1940, over a year after operation, there were several attacks of transitory left hemiplegia and he complained frequently of severe pain in the frontal and temporal regions of the head, worse on the right side. Compression for 5 minutes of the left carotid artery at the bifurcation

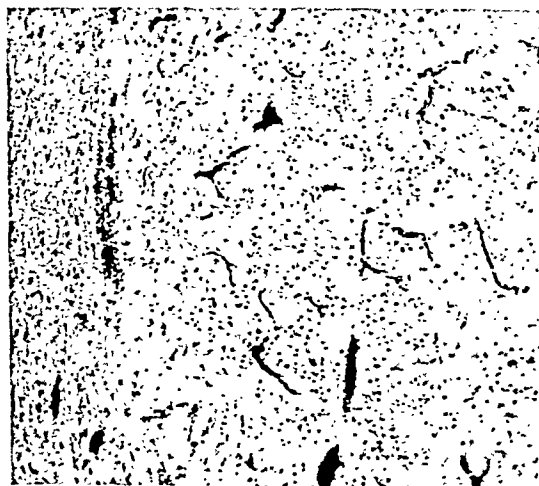


Fig. 14c. Case 4. A section through the cerebral cortex shows the marked increase in number and size of the small vessels of the gray matter. (Pal-Weigert stain,  $\times 35$ .)

diminished the intensity of bruit over the head 75 per cent and did not cause any untoward signs or symptoms.

Second admission to the hospital was on April 23, 1940. Because of the increasing symptoms and the apparent safety of occlusion of the carotid arteries on the left side of the neck, the child was brought back to the hospital for the purpose of ligation of these arteries.

Examination showed no essential changes from those recorded heretofore. The Rorschach psychometric test gave no indication of organic disease of the brain. Development was normal for his age except that the head was still disproportionately large and the left hemiplegia was more marked, the lower extremity was more palsied than the upper. There were no demonstrable changes in vision or in sensation. The bruit was distinct over the right side of the head, left eyeball, and left carotid in the neck, faint over the left side of the head and absent over the right eyeball. The blood pressure was 106/70 and the cardiac rate 70. The heart on roentgenogram was seen to have regained its original size and shape. The electrocardiogram was unchanged.

In preparation for operation the left carotids over the bifurcation were repeatedly compressed for 4 to 5 minute intervals for 4 days.

Cerebral angiography was carried out April 27, 1940, after the injection of 25 cubic centimeters of 35 per cent diodrast into the left common carotid artery. After ether inhalation anesthesia had been administered the left common carotid artery was exposed just below its bifurcation. The diodrast was rapidly injected in about 4 seconds and 3 roentgenograms were taken, one at the termination of the injection and 2 others at 7 second intervals.

The first roentgenogram (Fig. 11) showed the outline of some of the cerebral arteries on the left which appeared normal and the anomalous vessels of the right hemisphere which had been demonstrated previously after injection of thorotrast into the right carotid artery. No dye was visible on the second and third roentgenograms. No noteworthy incidents developed during or after the angiography and, since the child's condition appeared satisfactory on his regaining consciousness, he was returned to the operating room for ligation of the carotid arteries.

Operation was performed April 27, 1940. After resumption of ether inhalation anesthesia the left carotid arteries at the region of the bifurcation were exposed. These arteries were definitely larger than normal. After trial occlusion of the internal carotid for 20 minutes no unusual signs developed and the vessel was ligated with several strands of silk. The external carotid was ligated in similar fashion.

Samples of blood were taken from the left internal jugular vein before and again 10 minutes after occlusion of the left carotid arteries. The oxygen and carbon dioxide contents of the blood were as follows (see Case 3 for normal values). Before ligation of the arteries—oxygen content, 20.2 volumes per cent, carbon dioxide content, 48.8 volumes per cent. After

ligation of the arteries (10 minutes after)—oxygen content, 14.0 volumes per cent, carbon dioxide content, 55.6 volumes per cent.

There had been no noteworthy changes in the child's general condition during the operation and at its termination the pulse rate was 130, blood pressure 130/60, and respiration normal. The bruit could not be heard over the head but was of medium intensity over the eyeballs. Recovery from anesthesia was slow but no alarming signs developed until 4 hours after operation when twitching movements began in the left side of the body. Complete consciousness was not regained but there was restless movement of the head and right extremities and response to painful stimuli. The left sided convulsive movements occurred at first about every 5 minutes and lasted 10 to 30 seconds but gradually they increased in frequency and became almost constant. Occasionally there were convulsive twitchings of the right side as well.

On April 27, 1940, 6 hours after the carotids had been ligated the child was returned to the operating room for removal of the ligatures. The wound in the left side of the neck was reopened and the occluding ligatures on the carotid arteries were removed. There had been no injury to the vessel walls and there was no evidence of thrombosis for the arteries promptly filled with blood and pulsated briskly. There was also prompt improvement in the quality of the pulse and respiration, relaxation of the extremities, and subsidence of convulsive twitchings.

Although there was temporary improvement after removal of the ligatures occluding the carotids, within several hours the convulsive twitchings became more frequent and involved all extremities. There was marked rigidity of the extremities, pulse rate rose to 200 per minute, blood pressure was unobtainable, and temperature rose to 41 degrees C. The condition remained critical and various supportive measures were ineffectual. Death occurred 3 days after operation, April 30, 1940.

Postmortem examination was limited to the brain and the thorax. A section of liver was also removed for study. Before the skull was opened the left internal carotid artery and internal jugular vein were cannulated and the vessels of the brain were suffused first with saline solution and then with 10 per cent formalin. After the brain had fixed *in situ* it was removed together with the dura. The foramen spinosum on the right measured 3 millimeters and on the left 1.5 millimeters in diameter. The right internal carotid artery at the foramen lacerum measured 3 millimeters in diameter and the left 5 millimeters.

The surface of the entire right frontal lobe was covered with many thin walled vessels of various sizes (Fig. 12). There were numerous short vessels of 1 to 2 millimeters in diameter connecting these cortical vessels to the dura and presumably to the dural arteries. The gyrus of the right cerebral hemisphere particularly in the frontal lobe were smaller than those on the left and the entire right hemisphere was smaller than the left. Fluid injected into the

right internal carotid artery at the circle of Willis quickly distended some of the larger vessels on the lateral surface of the right frontal lobe but more complete injection of all the vessels was prevented because of tears in the walls of some. Fluid injected into the left internal carotid was seen to pass readily across the relatively large anterior communicating artery and into the vessels over the right frontal lobe.

Coronal section just behind the tip of the temporal lobes showed the small size of the right hemisphere as compared to the normal appearing left hemisphere (Fig. 13). The entire aspect of the cut surface of the right side was dark and many abnormal vessels were seen throughout the gray and white matter as well as in the corpus callosum on that side.

The brain nowhere showed any thrombosis of the vessels or evidence of recent hemorrhage.

The heart weighed 160 grams. The right ventricular wall measured 2 millimeters in thickness and the left 10 millimeters. Apart from slight dilatation and hypertrophy, the heart was usual in appearance.

Microscopic examination (Figs. 14a, b, c) revealed the following: Sections through the cortex of the right frontal lobe showed many superficial veins and a few arteries, all of large caliber, thin walled, and irregularly shaped. In the substance of the brain, particularly in the white matter, were numerous, often closely placed, large and small blood channels, the majority of which resembled veins. The thickness of the walls of these vessels varied greatly and was not uniformly in proportion to the size of the lumen. In some veins with relatively thicker walls the thickening of the media suggested faulty attempts at arterial structure. Elastic tissue stains showed a comparatively few of the vessels possessing definite *elastica interna* but in many there were delicate elastic fibrils scattered throughout the walls. The capillaries of the gray matter in particular, were greatly distended with blood. The vessels were mostly separated by interstitial tissue in which varying quantities but no notable increase of glial fibers existed. In places there were distinct areas of necrosis containing phagocytes and many small blood vessels in the interstitial tissue particularly in the cortical gray matter. Nowhere was there thrombosis or calcium deposit.

The tissue of the liver was of normal appearance except that, in many places in the periphery of the lobules and around the central veins, were small, unevenly deposited masses of brown granular material. This material, the deposited thorium compound, appeared to be inert and was unattended by any significant changes in the adjacent tissue.

While the child's first recognized episode of transient hemiparesis followed a few weeks after a fall and a bump on the head, there is no justification for ascribing the cerebral arteriovenous aneurysm to trauma. There is every indication that the lesion is a congenital one, though it is interesting to speculate on why



Fig. 15. Case 5. Lateral view of the skull showing in particular the local areas of rarefaction in the parietotemporal region resulting from direct pressure of the vessels of the aneurysm. Note fine calcified shadows in central region.

there were no neurological signs before the age of  $2\frac{1}{2}$  and indeed how and why attacks of hemiparesis occurred at all. Since these aneurysmal formations have a reputation for bleeding, the first thought was that the attacks resulted from recurring hemorrhage. It may be that small subpial hemorrhages were responsible but there were none of the clinical signs of subarachnoid hemorrhage at any time and the cerebrospinal fluid was found to be clear a short time after one of the attacks. Thrombosis of some of the vessels is also a possible explanation of the attacks for it has been known to occur spontaneously in such lesions and in fact is the principle upon which roentgenotherapy is based in the hope of obliterating the lesion. However, in the sections examined after death no thrombosed or obliterated vessels were encountered.

The injection of thorium dioxide on one occasion and diodrast on another served not only to verify the diagnosis but also to give some idea of the location, size, and extent of the vessels of the aneurysm. The thorium observed in the sections of the liver appeared after 15 months to be inert and to have caused no demonstrable local effects in the tissue. Diodrast gave an outline of the intracranial vessels equal to that produced by the thorotrast, and there is no indication on clinical or pathological findings that the injection of diodrast was a contributing factor in the child's death.



Fig 16. Case 6 Lateral view of the skull showing local area of rarefaction in the parietal bone due to pressure from a large vessel of the aneurysm (see also Fig 17).



Fig 17 Case 6 Retouched photograph taken at the operating table. Arrow points to the vessel which caused thinning of the dura and erosion of the skull seen in Figure 16. Inset indicates the site of the operative exposure.

It is assumed that the principal value of occlusion of the carotid arteries lies in the diminution of the total arterial supply to the aneurysm, thus easing the strain upon the thin walled veins and lessening the possibility of their rupture. It proved after the first operation in this case to have the additional value of taking sufficient load off the heart to diminish its size.

Since the successive occlusion of the carotid arteries in Case 3 had been uncomplicated no difficulties were anticipated in this case. Cerebral anoxia which undoubtedly caused death might have been avoided had but one artery, either the internal or the external (or the common) carotid on the left, been occluded at a time instead of both of the former.

CASE 5 Weakness, unsteadiness, underdevelopment of right extremities since infancy and daily headaches for one year in girl, 14 years old. Cephalic bruit, prominent vessels of the scalp and right hemiparesis found on examination. Calcified areas in left cerebrum. Distortion of ventricles and of sulcal markings seen by pneumo-encephalography. Ligation of left common and external carotid arteries. Diminution in bruit and improvement of headaches 1½ years later. On April 10 1939, Marie L., a 14 year old school girl, referred by Out Patient Department, was admitted to hospital complaining of headache, weakness and tremor of right extremities.

The girl's birth was uncomplicated but since infancy it was noticed that the right upper and lower extremities were weak, clumsy, and tremorous, she learned to use her left hand although it was supposed that she was naturally right handed. She had never had a convulsion.

A year before admission she developed recurring, severe, left frontotemporal headaches. They came almost daily, usually appearing the first thing in the morning, and lasting 2 to 3 hours. They were dull, throbbing, and occasionally associated with nausea.

Examination disclosed a quiet, intelligent girl who walked clumsily with the right leg and held the right arm close to the side. Speech was normal. The head was thought to be slightly larger than normal but not enough so as to distort her appearance. The vessels of the scalp in the left frontotemporal region were prominent and pulsating. There was no prominence or pulsation of the eyeballs. A bruit of low intensity was heard over the left frontotemporal region, less distinctly over the right side of the head, but equally over both eyeballs. The patient was unaware of any noise in the head. The vessels of the neck pulsed excessively. A faint thrill was felt on light palpation over them and a bruit was heard on auscultation, these signs were greater on the left. The left pupil was slightly larger than the right but there was some variation in this finding. The vessels of the left retina were full and tortuous in comparison to those on the opposite side but otherwise the optic fundi were unremarkable. Visual acuity and perimetry were normal. The right extremities were both slightly underdeveloped in musculature and weaker in strength but of normal lengths. There was a gross, ataxic intention tremor of these extremities and sometimes slow, vermicular adventitious move-

ments of the hand. There were slightly increased resistance to passive stretch, exaggerated deep reflexes, and an extensor plantar response on the right side. The blood pressure averaged 100/50 in each arm. The pulse had a full bounding quality and a rate of 90. The cardiac findings were normal.

Blood and urine tests were normal. Roentgenograms of the chest showed nothing abnormal in the lungs, heart, or great vessels. The spinal fluid was under normal pressure and the laboratory findings on the fluid were within normal limits; the total protein content was .030 grams per cent.

Roentgenograms of the head showed slight enlargement of the cranial vault. The skull was thin, and the frontal sinuses were large, the left greater than the right. There were no signs of increased intracranial pressure. The vascular markings of the skull (diploe) were moderately accentuated on both sides, particularly in the frontal regions. The grooves for the middle meningeal arteries were accentuated and more so on the left than on the right. The foramen spinosum was not well visualized on either side. There were several areas of rarefaction in the left parietotemporal region, imprints of large vessels of the aneurysm (Fig. 15). There were numerous small calcified areas in the subcortical region of the left parietal lobe.

Pneumoencephalography was performed April 25, 1939. Seventy-five cubic centimeters of air were injected after an equal amount of fluid had been removed. Roentgenograms showed the air in the subarachnoid spaces over the left cerebral hemisphere to have a curious, mottled appearance unlike the shadows marking the normal sulci on the opposite side. The ventricles were not shifted but the left lateral ventricle filled poorly and had irregular, distorted outlines.

Cerebral angiography was done on April 27, 1939 after the injection of 15 cubic centimeters of thorium dioxide solution into the left common carotid artery. Rapid injection was done in the usual way and roentgenograms were taken in 4 seconds, 12 seconds, and 18 seconds, after the injection, but only in the first plate were scattered flecks of the material seen in left parietal region.

Operation was performed April 29, 1939. With the use of local infiltration of procaine, occlusion of the left common carotid artery was accomplished by ligation with a strip of autogenous fascia lata, and the left external carotid artery was occluded with a double silk ligature. These arteries were estimated to be half again their normal size.

Samples of blood were taken from the left internal jugular vein before and 10 minutes after the arterial ligations. The oxygen and carbon dioxide contents of the blood were as follows (see Case 3 for normal values): Before ligation of the arteries—oxygen content, 15.5 volumes per cent; carbon dioxide content, 48.7 volumes per cent. After ligation of the arteries (10 minutes after)—oxygen content, 12.8 volumes per cent; carbon dioxide content, 50.1 volumes per cent.

There were no untoward reactions following operation, no change in power or sensation on the right side of the body, no visual perimetric defects and no difficulty in speech. There was no change in the blood pressure or pulse. The bruit heard over the head was estimated to possess about one-half its former intensity. The bruit over the left eyeball was hardly audible while over the right eyeball the intensity was as great if not greater than originally.

During the first 3 months after leaving the hospital she had three convulsive seizures, each characterized by the successive appearance of inability to speak, paresthesias on the right side of the body, inability to move the right extremities, inability to see to the right, loss of consciousness for 5 to 10 minutes (without known convulsive movements) and headache on the left side of the head upon recovery. Phenobarbital in 15 milligram doses three times a day was prescribed after the second attack but later discontinued. No further convulsions occurred during the 18 months after operation.

The bruit over the head remained faint and was barely perceptible over the left eyeball, yet over the right eyeball it was loud. Compression of the right common carotid artery caused the bruit everywhere to become barely audible and after 4 minutes of compression there were no signs of cerebral anemia.

The headaches were markedly improved following ligation of the carotids and, since this was the complaint for which she requested relief, she was well satisfied. There were occasional headaches, less severe than her former ones, and on one occasion the injection of half an ampul (.25 mgm.) of ergotamine tartrate caused the pain to disappear promptly.

It is interesting that this child had sufficient damage to the left cerebral hemisphere to cause hemiparesis since infancy, yet had had no convulsive seizures until after the ligation of the carotid arteries. The ligation resulted in definite and sustained diminution in the intensity of the bruit and possibly thrombosis occurring in some of the smaller vessels of the aneurysm was the cause of the convulsions. Although the carbon dioxide and oxygen contents of the jugular blood returned to normal after ligation of the arteries, doubtless had additional samples been taken later, the improvement would be less marked since there was evidence of the persistence of the aneurysm. Still another noteworthy finding here was that no cerebral vessels were visualized by angiography though the test was performed as it always has been when satisfactory visualization of the vessels has resulted. The circulation time through the left hemisphere in this case may have been so rapid, due to direct

dumping of arterial blood into large venous channels, that the material injected was too rapidly diffused to cast a shadow.

**CASE 6.** Left sided convulsions for 6 years in man 42 years old. Cephalic bruit, not discovered before operation. Distortion of the ventricles seen by ventriculography. Arteriovenous aneurysm of right frontoparietal area of brain disclosed by osteoplastic exploration. Subtemporal decompression. Improvement in convulsions one year later.

On October 25, 1939, Edward R., aged 42, a clerk, referred by the Out Patient Department was admitted to the hospital, complaining of convulsive seizures for 6 years.

At the age of 36 he had his first convulsive seizure. It started in the left side of the neck with a tight seching which spread to the face and arm on the same side. It was followed in a few minutes by loss of consciousness and a generalized convulsion involving mostly the left side of the body. Fourteen others occurred in the next 6 years and all followed the same pattern except that sometimes the onset was in the face or roof of the mouth on the left. All attacks were diurnal. The attacks lasted 15 to 20 minutes and were followed by drowsiness. He never had headache or any other significant symptoms.

Examination revealed nothing remarkable in his general physical condition and his mental attributes were above average. There were no nevi or abnormal pigmentations over the body. Blood pressure averaged 122/80 in each arm and the cardiac rate was 80. The heart findings were normal and the pulse was of normal quality. There was a faint bruit over the right frontoparietal area of the head, over both eyeballs, and over the right carotid artery (not discovered until after operation). The patient was unaware of the bruit. The carotid arteries in the neck were not unusual on palpation. There was no enlargement or pulsation of the vessels of the scalp and the retinal vessels were not remarkable. Other functions of the head were normal as were motility and sensory functions over the body. Reflexes were normal except for slight increase of those in the left upper extremity.

Blood and urine tests were normal. Electrocardiogram showed moderate left axis deviation indicative of hypertrophy of the left side of the heart but a roentgenogram of the heart showed only slight enlargement to the left.

Roentgenogram of the skull (Fig. 16) showed a normal vault but some thinning of the bone of the right parietal region. The frontal sinuses were large, the right larger than the left. There were no signs of increased intracranial pressure but there were oval shaped areas of rarefaction in the right parietotemporal area due to pressure of the large vessels of the aneurysm. Also the vascular markings of the cranium (diploe) were accentuated, and the groove for the right middle meningeal artery was deeper and wider than usual.

Lumbar puncture (in horizontal position) showed an initial spinal fluid pressure of 150 millimeters of water and normal rise and fall of the pressure on jugular compression. The examination of the fluid showed a total protein of 0.40 grams per cent.

The electroencephalogram showed pathological waves in all frontal leads without lateralizing signs.

Ventriculography was carried out November 15, 1939. Twenty cubic centimeters of clear fluid were exchanged for air. Roentgenograms showed irregular filling of the body of the right lateral ventricle and slight depression of the right frontal horn, also, slight shift of both lateral ventricles and the third ventricle to the left.

The supposition was that the lesion was possibly a small right parietal meningioma.

Operation was performed November 15, 1939. After ether anesthesia had been administered, a right parietal osteoplastic operation was performed. Neither the scalp nor the bone was found to be unusually vascular and the dura was not adherent to bone. However, the middle meningeal artery was tortuous and twice the usual size. At one place the dura was humped up, thinned out, and bluish in color because of a large, pulsating cortical vessel beneath. It was this vessel that had caused the prominent area of erosion in the bone and the depth of the depression in the bone was about 5 millimeters. Elsewhere the dura had a wavy appearance as it was humped up by other large vessels beneath it and there were shallower depressions in the bone corresponding to some of these vessels. Since the bruit over the head had not been detected before operation, a stethoscope was sterilized and placed upon the dura, a loud systolic bruit was audible. The dura was reflected from the brain and numerous adhesions between the dura and the pia arachnoid were encountered. Some of the adhesions were flimsy and broke easily, others were so tough they required cutting. Only in one place was a vessel seen to pass directly from a cortical vessel to the dura. However, this anastomotic vessel was as large as the middle meningeal artery.

The surface of the brain thus exposed (Fig. 17) was largely covered by a tangle of reddish, tortuous, and pulsating vessels. Several of the largest vessels (8 to 10 mm in diameter) extended from the depths of the lateral cerebral fissure obliquely across the field in the line of the Rolandic fissure. Elsewhere over the surface the vessels were smaller. But anteriorly there was a compact mass, about 3.5 centimeters across, of small (1 to 2 mm) vessels, which had an angiomatous appearance. The midcerebral artery, identified deep in lateral cerebral fissure, was fully three times its usual size at this location.

A faint thrill was detected by palpation of the large vessels and their thin walls made it possible to see blood swirling through them with each pulsation. Obviously these larger vessels were veins containing arterial blood. Compression of the right common or of both common carotid arteries in the neck caused an immediate decrease in the flow of blood through

these vessels and some even became promptly smaller but filled out again in a short time even though the pressure was maintained. No difference could be detected in the effects of compression of the right carotid from the effects of simultaneous compression of both carotid arteries. Compression of the left artery alone caused no visible change in the blood flow or in the size of the vessels.

The patient had two convulsive seizures during the time the cortex was exposed. They consisted of contraction of the left side of the face and upper extremity with a few clonic motions but no loss of consciousness. Preceding, during, or after the attacks no visible change in the vessels occurred. Both attacks stopped promptly after compression of the right carotid artery in the neck.

Faradic stimulation was applied to many points over all of the exposed vessels, even to those low in the lateral cerebral fissure, but no pain was elicited. The middle meningeal artery was widely pain sensitive.

No attempt was made to ligate any of the cortical vessels. A subtemporal decompression was made, a piece of the middle meningeal artery and dura was taken for microscopic study and the bone flap was replaced and sutured.

Microscopic examination of the section of the meningeal artery removed for study disclosed early arteriosclerotic changes but no other changes of note. Recovery was uncomplicated and the patient was discharged 2 weeks after operation without medication for convulsions. The decompression was flat. In the year after operation he had two convulsions both following debauches of drinking. He considered himself improved because these convulsions were not severe and he had had six severe seizures in the year prior to operation.

The diagnosis should have been suspected before operation by the history of lateralized convulsive seizures and the curious vascular markings of the skull disclosed by roentgenogram, even though the bruit over the head was overlooked.

Two important facts were disclosed during the operation: one, that the flow of blood through the vessels of the aneurysm is definitely affected by compression of the carotid arteries in the neck though mostly by the one on the side of the lesion; the other, that the vessels of the aneurysm are not pain sensitive. Since this patient had no headache the latter finding would appear to have no great significance and in fact normal vessels in the same region have no pain sensitivity (20), yet it does have value in arriving at an interpretation of the localized headaches that have occurred in 2 other patients.

Because this case was much like that of Case 1 in which there was benefit from decompression alone it was thought best not to pursue the treatment here beyond simple decompression, at least to begin with. In the event of the return of frequent convulsions, both ligation of the right carotid arteries and roentgenotherapy will be advised.

#### DISCUSSION

The discussion will be limited to a consideration, principally, of the cerebral arteriovenous aneurysms which are typified by the 6 cases of this series and no attempt will be made to review exhaustively all the literature dealing with the subject. Also, since others have dealt fully with the differentiation and symptomatology of these and other vascular malformations of the head, emphasis will be put largely upon those aspects of the lesion—pathological, symptomatic, diagnostic, and therapeutic—that may supplement or refute past experiences and impressions.

#### THE NATURE AND SPECIFIC MANIFESTATIONS OF CEREBRAL ARTERIOVENOUS ANEURYSMS

*Etiology.* As pointed out by Dandy, it is unlikely that the arteriovenous aneurysms of the brain could result from trauma since the principal arteries and veins are not in juxtaposition as are the vessels of the extremities and elsewhere. In addition, the form in which these lesions occur is evidence of their congenital origin. They are composed of (a) an arterial side, the inlet, (b) a venous side, the outlet, and (c) multiple short communications or an interposing bed of racemose vessels. These latter vessels are malformations and are the counterpart of the normal capillary bed between arteries and veins. They have been found on microscopic examination, as in Case 4, to be both arteries and veins (3). Some authors have suspected that a venous malformation exists first which later becomes arterialized (1) but were this true arteries would not be expected in the "nests" of vessels just described.

*The gross appearance.* There is no mistaking these spectacular lesions when they are exposed at the operating table. One sees large, pulsating and tortuous veins, some



centimeter or more in diameter, lying on the surface of the brain, and swirls of blood showing through their thin walls with each pulsation. The swirling appearance is due to the bright arterial blood mixing with darker venous blood and a dull red color is lent to the entire vessel which is the color neither of normal veins or arteries. The size of these veins varies, depending upon how directly the arteries empty into them. Thus, if the connecting vessels are few and of larger caliber, larger veins will result than if the arterial blood has first to pass through a greater number of smaller vessels. In the 4 cases subjected to exploratory operation not all the vessels were exposed in the operative fields but a comparison shows that in 2 of the cases in which the veins were largest there were fewer of the smaller vessels in evidence. It may be assumed that many veins both on the surface and in the substance of the brain undergo dilatation in the presence of an arteriovenous aneurysm because the arterial pressure must be dissipated in the venous system. As a matter of experience, it has been established that the external cerebral venous system is more characteristically implicated than the internal, though in Steinheil's case the veins of Galen were enlarged. The fact that the veins of the retina, in some cases, are distended indicates, however, that veins at a considerable distance are secondarily affected by the increase in the intracranial venous pressure. In Case 4 even the internal jugular vein was definitely large and pulsating.

The small connecting vessels also present an impressive sight in the form of tangled masses or "nests" of closely packed, pulsating arterioles and venules. On the whole, they have a redder color than the large veins but are usually still distinguishable from normal arteries. These more or less discrete masses of vessels have a tumorous appearance and no doubt have been the reason in the past for considering the lesions "angiomas." It is in these vessels that thrombosis and calcium deposits occur and doubtless changes of this nature predispose to rupture and hemorrhage.

The arteries that supply the fistula are themselves enlarged, sometimes to two or three times normal size. This is the result of

a phenomenon which is spoken of as the "venification" of the artery proximal to the fistula. The arterial wall thins out due to diminution of elastic tissue, loss of muscle fibers in the media, and stretching of the normal elements. It is supposed that the lowered peripheral resistance diminishes the degree of recoil and contraction of the artery and is the contributing factor in these atrophic changes (13). In Case 6 the mid-cerebral artery low in the lateral cerebral fissure was fully three times normal size and in the aneurysm of Case 3 the mid-cerebral artery was nearly as large as the internal carotid. In the illustration of Dennis' case (3), numerous arteries at the base of the brain were dilated but this is only to be expected since the carotid arteries in the neck and even the heart have been found to be enlarged (Cases 3, 4, and 5).

*The cardiovascular effects.* The effects upon the cardiovascular system of a cerebral arteriovenous aneurysm may be far reaching. This is a principle that has been well established by the now comparatively wide experience with arteriovenous fistulas elsewhere in the body in man, and also with experimental fistulas in lower animals. The effects, after the experimental production of arteriovenous fistulas, have been summarized admirably by Holman (12) and may be profitably quoted.

"The production of an arteriovenous fistula establishes two systems of circulating blood (A) the heart-artery-capillary bed vein system, and (B) the heart artery-fistula vein system. The short circuiting of a volume of blood through system (B), with its greatly reduced peripheral resistance, introduces a large factor of inefficiency into the circulatory system with particular reference to blood pressure. The variable factors concerned in the maintenance of blood-pressure are (1) cardiac output, (2) total volume of circulating blood, (3) capacity of system, (4) peripheral resistance.

"The lowered peripheral resistance in the presence of a fistula is compensated by changes in the remaining three variable factors, and in this way only is an adequate blood-pressure level maintained.

"The volume of blood diverted and short-circuited through the lowered resistance of the fistula depends entirely on the size of the fistula, and the absence of any obstruction in the venous return flow to the heart proximal to the fistula. A small communication produces only slight changes, and these may not be detectable. Without present instruments of precision the slight alterations necessary to compensate for a small leak are not demonstrable, nor do

they produce any visible visceral changes. A slightly larger fistula may result in changes, only some of which are demonstrable. A fistula larger in size than the feeding artery, or large enough to divert a considerable flow back to the heart, invariably produces demonstrable changes, both immediate and remote. That these changes to a greater or lesser degree occur in the presence of every fistula, no matter what size, seems beyond question, the extent in each case depending entirely on the volume of blood diverted through the fistula.

"The immediate changes due to the production of a fistula are: (1) A fall in general arterial blood pressure affecting both systolic and diastolic levels; (2) an increase in pulse rate; (3) an increase in venous pressure, proximal as well as distal to the fistula, which is slight or pronounced, according to the size of the fistula.

"The remote effects following the production of a fistula are: (1) A permanent diversion of part of the blood volume from the circulatory system of heart-artery-capillary bed-vein into the second circulatory system of heart-artery-fistula vein. (2) A gradual increase in the amount of blood volume flowing through the new system, heart-artery-fistula vein, depending on the size of the fistula. (3) A gradually increasing vigor of heart action. (4) A gradually increasing total blood volume, proceeding *pari passu* with the amount of blood diverted through the fistula. (5) A gradual dilatation of the heart, and of the artery and vein proximal to the fistula, to accommodate this increasing flow of blood through the fistula. (6) Hypertrophy of the heart due to the increased work necessary to propel forward this increasing volume of blood flowing through it. (7) A gradual recovery from the lowered blood-pressure noted immediately after the formation of the fistula, the systolic equal or higher, the diastolic definitely lower than that existing before the formation of the fistula, thus producing a greatly increased pulse-pressure."

While many of the principles set forth in this summary are more or less applicable to the cerebral arteriovenous aneurysms under consideration, it is to be noted that on the whole the effects upon the cardiovascular system of the cerebral lesions are much less pronounced or dangerous to life than those that result from, say, an acquired aneurysm between the femoral artery and vein. The acquired fistulas of the carotid artery and cavernous sinus are more like the fistulas of the extremities in this respect. In one, the congenital origin of the lesion permits compensation from embryo, while in the other, compensation is more complicated. In addition, the amount of stress put upon the general cardiovascular system is directly proportional

to the size of the artery and of its opening into the venous system. The mid-cerebral artery, which is the cerebral artery most frequently implicated, is several times smaller than an artery such as the femoral and the malformation of many small vessels between the cerebral artery and the cerebral veins has the effect of minimizing the size of the fistula.

In this series, Cases 2 and 4 had demonstrable enlargement of the heart with changes in their electrocardiographic records, while Case 6 had only electrocardiographic changes. Case 4, that of the 2½ year old child, showed the greatest changes in the cardiovascular system of all, and since there is no reason to assume that there is any essential difference between his aneurysm and the others it may be deducted either that, because of some unknown factors, he failed to compensate well or that in due time compensation might have been effective. This child also had the most pronounced elevation of pulse pressure in the series; Cases 1, 3, and 5 might be said to have slight elevation of pulse pressure. In Case 2, that of a 43 year old woman, the clinical picture was of hypertensive cardiovascular disease, and rather than attempt to explain her findings on the basis of the arteriovenous fistula it may be assumed that not only had she long since compensated for the fistula but had fortuitously developed hypertension. In the cases in which the carotid arteries in the neck were exposed (Cases 3, 4, and 5) these arteries were estimated to be enlarged; the finding was most pronounced in Case 4 and in the same case the internal jugular veins were also enlarged. The pulse rate was not unusual in any of the cases though in 4 the quality of the radial pulse was distinctly full and bounding and in Case 4 suggestive of a "Corrigan pulse."

*The collateral circulation.* The powerful stimulus to the development of a collateral arterial circulation imposed by an arteriovenous fistula is evident in individuals having cerebral arteriovenous aneurysms. Enlarged, tortuous and pulsating arteries of the scalp as well as enlarged middle meningeal arteries have been observed commonly in these individuals. In Cases 1, 3, 4, and 5 the arteries of the scalp, and in Cases 1, 2, 3, and 6 the middle meningeal arteries exposed at operation

## SURGERY, GYNECOLOGY AND OBSTETRICS

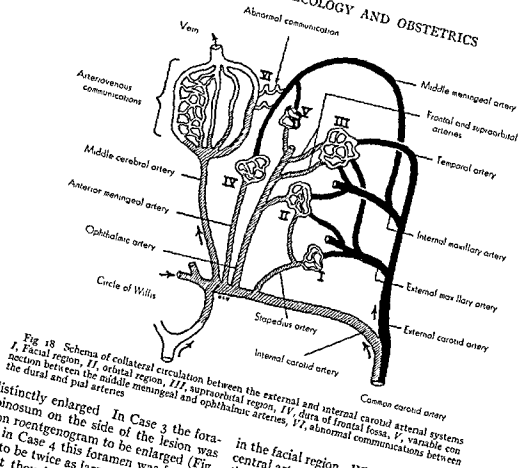


Fig 18 Schema of collateral circulation between the external and internal carotid arterial systems. I, Facial region, II, orbital region, III, supraorbital region, IV, dura of frontal fossa, V, variable connection between the middle meningeal and ophthalmic arteries, VI, abnormal communications between the dural and pal arteries.

were distinctly enlarged. In Case 3 the foramen spinosum on the side of the lesion was shown on roentgenogram to be enlarged (Fig 4b) and in Case 4 this foramen was found at autopsy to be twice as large as its mate.

On first thought it is difficult to see how there can be readily established a collateral circulation between the branches of the external and internal carotid arteries since the two are often thought of as distinct and separate arterial systems. But the superficial temporal artery, a terminal branch of the external carotid artery, has rich anastomosis not only with the corresponding artery from the opposite side of the head but also with the supraorbital and frontal arteries which are terminal branches of the ophthalmic artery, itself a branch of the internal carotid (Fig 18). Many other anastomotic relationships exist with the branches of the internal carotid in the orbital region, and also with the branches of the external carotid in the facial region. With the exception of the central artery of the retina, all the branches of the ophthalmic artery communicate with some division of the external carotid, the principal ones being the external maxillary, the principal maxillary, and the superficial temporal arteries. The middle meningeal artery, an anastomosing branch of the external carotid artery, one of which originates directly from the internal carotid and the others from ethmoidal branches of the ophthalmic artery. Wolf has called attention also to the communication of branches of the external carotid in the face with the stapedius artery, a branch of the internal carotid.

Connection may exist between the middle meningeal and the ophthalmic arteries through a variety of anomalies, for in some lower animals the ophthalmic arises wholly from the meningeal and vestiges of this arrangement persist in man (27, 32).

## RAY: CEREBRAL ARTERIOVENOUS ANEURYSMS

In addition to the collateral circulation between the external and internal carotids which utilizes the normal arrangement, often there is found the unique development of vessels that pass directly from the cerebral aneurysm to the overlying dura and the meningeal arteries. In all of the 4 cases in which cerebral exploration was performed and in the case with postmortem examination, these anastomotic vessels were seen. In Case 6 but one such vessel was encountered whereas in the others a number of short, and sometimes large calibered, aberrant vessels were present.

The external carotid arteries of the two sides are connected by numerous unions between the lingual, external, maxillary, occipital, posterior auricular and ascending pharyngeal arteries which make up abundant peribuccal and peripharyngeal circles. The external carotid arteries also possess efficient anastomotic communication with the thyrocervical and the thyroid arteries principally and with the costocervical trunks via the occipital arteries. Case 3 exemplifies the most extensive interruption of the blood supply to the brain by ligation of the internal and external carotid arteries on each side of the neck and one superior thyroid artery. Here it is to be assumed that while the vertebral arteries comprise the principal supply to the brain it must still receive some arterial blood through the internal and external carotid arteries whose more distal branches communicate with branches of the thyrocervical and costocervical trunks.

*The bruit and thrill.* The bruit and thrill accompanying arteriovenous aneurysms have been attributed to various causes but the most acceptable explanation is that they result from vibration of the walls of the vessels. The vibration is produced by alternating currents of blood under high and low pressure (13). In all 6 of the cases of this series a bruit was detected first or last by auscultation over the head and neck. In the first 2 cases, due to what Cushing and Bailey (3) termed a "strange human frailty," auscultation of the skull was not a part of the preoperative examination and the bruit was not heard until after the nature of the lesion had been established by operation. In the next 3 cases auscultation was a part of the examination of the head and the

bruit was readily detected. But in the sixth case, although several observers auscultated the head, the bruit was overlooked. Doubtless, the size and the individual arrangement of a cerebral arteriovenous fistula has some effect upon the intensity of the bruit, yet it is likely that if listened for carefully, a bruit will always be detected somewhere over the head when the lesion is present. It was loudest, in all 6 cases, in that region of the head that overlay the lesion, but in 2, it was also heard over other parts of the cranium. The bruit heard over the eyeballs was sometimes more distinct than that heard over the skull, although in Case 2 it was heard only faintly over the homolateral eyeball. A bruit was also heard over the carotid arteries in the neck in 5 cases; in the 2 children it was present over both sides but loudest on the side of the lesion.

The presence of a bruit over the carotid arteries in the neck is probably the result of the transmission through the vessels of the cerebral aneurysm. The jugular veins could contribute little or nothing to the sound since the internal jugular vein exposed in 3 individuals was found in only 1 to be unusually large and tense. In this latter case the bruit in the neck disappeared after ligation of the carotid alone.

The bruit heard over the eyeballs must be similarly dependent upon transmission of the sound through blood vessels of the orbit. The ocular bruit, and also the pulsating exophthalmos, associated with the fistulas between the carotid artery and cavernous sinus appears to be dependent principally upon the veins of the complex while the ocular bruit associated with the cerebral lesions under discussion are dependent in large part upon the arteries of the orbit. Furthermore, the arterial collateral circulation through the orbit, already discussed, probably contributes chiefly to the transmission of the bruit. This conclusion is suggested principally by the fact that occlusion of the internal and external carotid arteries on one side (Cases 3, 4, and 5) caused almost complete disappearance of the bruit over the homolateral eyeball but did not affect that heard over the contralateral globe. Additional and perhaps more conclusive evidence was afforded by the finding, in Case 3, that ligation

**SURGERY, GYNECOLOGY AND OBSTETRICS**  
**TABLE I—ANALYSIS OF THE AUTHOR'S SIX CASES OF CEREBRAL ARTERIOVENOUS ANEURYSM**

	Frank B., No 121609 41 yrs—M	Helen R., No 127311 41 yrs—F	Mike B., No 146472 20 yrs—M	George S., No 121813 3 yrs—M	Marie L., No 127011 14 yrs—F	Edward R., No 105151 41 yrs—M
History of trauma	No	No	No	Questionable	No	No
Site of lesion	Left fronto-parietal	Right parietal	Right fronto-parietal	Right fronto-parietal	Left parietal	Right parietal
First symptom and age of onset	Generalized headache at 4 yrs	Paresthesias of left hand at 40 yrs	Convulsions at 14 yrs	Transient left hemiplegia at 3½ yrs	Hemiparesis since birth	Convulsions at 3½ yrs
Symptoms (and age of onset)	Convulsions	Generalized, averaged 2 a year Began at 26	Left sided petit and grand mal at 41	Left sided petit and grand mal	None	Only after ligation of carotid artery
	Falsy	No	No	No	Left hemiparesis	Right hemiparesis
	Paresthesias	No	No	No	Left hand and face	Left hand and face
	Headache	Generalized at 4 Left frontal, began at 38	No	No	No	No
Time of convulsions	3 nocturnal Others diurnal	Diurnal	1/4 nocturnal 3/4 diurnal	o	Daily left frontal Began 13 yrs	No
Increased vascularity of scalp	Yes	No	Yes	Yes	o	Diurnal
Mental changes	None	Panic state Paranoid psychosis	None	None	Yes	No
Bruit and location heard	Left frontal area Both eyeballs Not detected preoperatively	Right frontal area Right side neck Not detected preoperatively	Right fronto-parietal Both eyeballs Detected preoperatively	Entire head Both eyeballs Both sides of neck Detected preoperatively	Entire head (lt. > rt.) Both eyeballs Both sides of neck (lt. > rt.) Detected preoperatively	Right fronto-parietal Both eyeballs Over right side of neck Not detected preoperatively
Cardiovascular changes P B P E A G *	BP 118/70. P 70. Pulse quality normal Heart sounds normal EKG not done	BP 165/108 P 80 Pulse quality bounding Heart sounds normal Heart on x ray slight left enlargement. EKG left ventricular preponderance	BP 110/66 P 75 Pulse quality full Heart sounds faint systolic murmur Heart on x ray normal EKG normal	BP 104/70. P 70. Pulse quality bounding Heart sounds systolic murmur Heart on x ray enlarged superior vena cava. EKG left ventricular preponderance	BP 100/70. P 60 Pulse quality bounding Heart sounds normal Heart on x ray normal EKG normal	BP 118/80. P 80 Pulse quality normal Heart sounds normal Heart on x ray slightly enlarged to left EKG left ventricular preponderance
	Slight papilledema Full vessels bilaterally	Full, tortuous vessels right side	Full tortuous vessels on right side	Full, tortuous vessels both rt. > lt.	Vessels full and tortuous on left	Normal
X ray of skull	Increased vascularity of skull	Yes	Yes	Yes	Yes (slight enlarged head)	Yes
	Erosions due to pressure of vessels	Yes	No	No	Yes	Yes
Spinal fluid	Calcification in lesion	Yes	No	No	Yes	No
Cerebral arteriography	Pressure 220 mm Total protein, 0.50 gm %	Not studied	Pressure 200 mm Total protein 0.50 grams %	Normal pressure Total protein, 0.30 grams %	Normal pressure Total protein, 0.30 grams %	Normal pressure Total protein 0.40 grams %
	o	No	Yes	Yes	Unsatisfactory	No
Encephalogram or ventriculogram	Ventriculogram Depression of left frontal bone	Ventriculogram Irregularity of body of right lateral ventricle	Encephalogram Deformity of right ventricle and slight shift to left. Nothing over right hemisphere	Encephalogram Depression of right and slight shift to left. Nothing over right hemisphere	Encephalogram Poor filling and irregularity of left ventricle. Nothing over left hemisphere	Ventriculogram Small depressed ventricle, right

P, pulse B P, blood pressure E A G, electrocardiogram

TABLE I.—ANALYSIS OF THE AUTHOR'S SIX CASES OF CEREBRAL ARTERIOVENOUS ANEURYSM  
Continued

	Frank B., No. 137609 41 yrs.—M.	Helen R., No. 127311 43 yrs.—F.	Mike B., No. 126422 20 yrs.—M.	George S., No. 221823 3 yrs.—M.	Marie L., No. 227011 14 yrs.—F.	Edward R., No. 229121 42 yrs.—M.
Operation	Occlusion of carotid arteries No	No	Right common and external arteries 3-23-1930. Left internal carotid 11-24-1930. Left external carotid, 12-7-1930	Right common and external carotid 2-15-1930. Left internal and external carotids 4-27-1930	Left common and external carotids 4-29-1930	No
	Exploration and subtemporal decompression	7-20-1936	9-1-1936	10-10-1936	No	No
X-ray therapy	1,050 r units (inadequate)	10,200 r units over 15 mos.	13,200 r units over 25 mos.	0	0	0
Result of treatment	Fewer convulsions. Headaches stopped for 1 yr., then recurred with less severity over left frontal area	No improvement in mental state. Fewer convulsions	Cessation of grand mal convulsions. Fewer and slighter petit mal attacks	No improvement except diminution in size of heart after first operation. Death 3rd day after 2nd operation. Autopsy	Relief of headache	Fewer convulsions

\*P., pulse; B.P., blood pressure; E.K.G., electrocardiogram.

tion of the contralateral internal carotid caused marked diminution in the cephalic bruit but an increase in the bruit over the eyeball on that side; this bruit was greatly diminished, however, when the common carotid on that side was occluded, thus shutting off the principal supply to the external carotid artery. The shifting or intensification of the bruit to the unaffected side is mentioned by Singleton in his experiences in ligation of the carotids for intracranial arteriovenous fistulas.

It is an interesting fact that in none of the cases of this series did the patients complain of tinnitus or noise in the head prior to operation, nor could they detect any noise when told that one was present. Case 4, the child of 2½ years, may possibly be an exception. In cases reported elsewhere (1, 3), some patients have been aware of the bruit and it is probable that the location of the aneurysm has some influence upon this; the nearer to the petrous bone the more likely the patient is to be aware of it. Brock and Dyke ascribed the tinnitus in one of their patients to the auditory perception of the systolic bruit in the adjacent enlarged temporal artery. It was suggested by Cushing and Bailey (3) as quite conceivable that a decompression operation might serve to accentuate a sound which would otherwise be dampened by a closed cranial chamber, and this seems to have been the case in the last pa-

tient who detected a faint bruit for the first time after cranial exploration and subtemporal decompression.

*The location of the aneurysms.* In this series, all the aneurysms have appeared to be the result of an anomalous formation involving principally the mid-cerebral artery. In a majority of the collected cases the mid-cerebral artery has been concerned but the malformation may occur in arteries anywhere in the brain. The lesion's next most frequent location has been the occipital lobe, probably the result of malformation of the posterior cerebral artery, and other rarer locations have been the cerebellum (3, 4, 17, 34),<sup>1</sup> the corpus callosum (5), the corpus striatum (28), and the midbrain (1). In 1 case (33), besides the cerebellar lesion, there was a second and similar lesion in the parietal lobe.

#### THE INCIDENCE OF ARTERIOVENOUS ANEURYSMS OF THE BRAIN

Congenital arteriovenous aneurysms in all locations of the brain are said by Dandy to have a frequency of 0.5 to 1 per cent in clinics where neurological material is concentrated. In Cushing's (2) summary of 2,023 verified brain tumors the frequency of "angioma arteriole" was about 0.5 of 1 per cent. The comparatively low incidence of the lesion neces-

<sup>1</sup>See footnote on following page.

sarily limits any one individual's experience with it and it is a fortunate occurrence that in the short space of 4 years the 6 cases of this series (and 1 additional case<sup>1</sup> not included in this series) should have come under the author's observation and been available for frequent observations during that time.

Males seem to develop these lesions more often than females in a ratio of about 3 to 1; in this series the ratio is 2 to 1.

#### THE SYMPTOMS AND SIGNS OF CEREBRAL ARTERIOVENOUS ANEURYSM (TABLE 1)

*Onset.* It is a striking fact that although there is sufficient reason to believe the lesions to be congenital (24), symptoms often do not make their appearance or at least do not come to serious attention until comparatively late. Some have thought this to be evidence against their congenital origin. It suggests, rather, that the explanation for the tardy symptoms lies in the hypertrophic and the premature degenerative changes constantly occurring in the vessels of the lesion which in turn are accompanied by hemorrhage, by destruction of nervous tissue and possibly by an expansion in the volume of the vessels involved. Trauma might well serve to increase the size or produce other changes in a lesion already present just as trauma has been seen to enhance the growth of a cirroid aneurysm of the scalp (7). Cushing and Bailey (3) stated that to their knowledge the lesion had not been observed in infancy, yet one of the cases reported here is that of a child, 2½ years old, and the author has examined but does not have complete records of an 11 months' old baby whose symptoms and signs were undoubtedly those of a right cerebral arteriovenous aneurysm.

First symptoms and the age of their appearance in the cases of this series are listed as follows: Case 1, headaches since the age of 4 and first convulsion at 26; Case 2, attacks of paresthesia in the left upper extremity at 40; Case 3, generalized convulsion at 14; Case 4, transitory left hemiparesis at 2½; Case 5, right sided weakness since infancy; Case 6, convulsive seizure beginning in the left upper extremity at 36.

<sup>1</sup>One case of congenital arteriovenous aneurysm of the cerebellum has been encountered by the author and exposed at operation but is not included in this report which deals only with the cerebral lesions.

*Convulsions.* Convulsions were the first important symptom in but 3 of the cases though in all 6 convulsions eventually occurred. In all instances there was some clue before, during, or after attacks, as to the side of the body more affected, but there was no distinctive feature about the attacks that would stamp them as different from those caused by some other lesion in the parietal region of the brain. However, convulsions are not necessarily an accompaniment of any lesion that involves the paracentral area of the cerebrum, and it would be erroneous to insist upon the occurrence of convulsions for the diagnosis of a cerebral arteriovenous aneurysm.

*Focal signs and symptoms.* Transient hemiparesis, as occurred in Case 4, has been mentioned commonly in the reports of others, and the most reasonable explanation for such events is thrombosis or hemorrhage. A lumbar puncture performed within a few hours after the rapid development of hemiplegia in this patient failed to show any abnormality in the fluid; while thrombosis appears to be the most plausible explanation, no thrombosed vessels could be discovered on final examination of the brain. Doubtless the early appearance of unprogressive hemiparesis in Case 5 was the result of thrombosis or hemorrhage of the lesion in babyhood.

Other focal symptoms and signs that might reasonably be expected to occur with arteriovenous aneurysms of the cerebrum are sensory disturbances, aphasia (if the lesion is on the proper side) and visual perimetric defects. These were not present as constant findings in any of the cases though in Case 5 following ligation of the carotids, there were three convulsions which were preceded by aphasia and a right homonymous hemianopsia.

*Headache.* Headache was not an outstanding symptom in the records of the cases that have been reported by others and often, when mentioned, it was not qualified or thought important enough to ascribe to any particular mechanism. Increased intracranial pressure was perhaps the explanation of some instances of headache but not all, for intracranial hypertension was a comparatively infrequent development. Convulsions and subarachnoid hemorrhage were the causes of headache in

other cases. However, there is a group of cases remaining in which the headache cannot be ascribed to any one of these. In the light of increasing information with regard to the pain sensitivity of various intracranial and extracranial structures, and the mechanism by which headache can occur (20, 26), it may be profitable to consider the headaches associated with cerebral arteriovenous aneurysms not the result of the causes just mentioned.

The headaches referred to are typified by those described in Cases 1 and 5. They occurred periodically, sometimes daily, and usually appeared very soon after rising in the morning; they were localized over the frontotemporal region of the head on the same side as the aneurysm; they had a dull, painful, throbbing character and were associated with nausea; they lasted for several hours at a time. In Case 1 the headache was preceded by pain which began low in the neck and progressed upward into the side of the face and finally localized in the head. A case fully described by Brock and Dyke was very like these and the headache was said to be migraine but thought not to be related to the cerebral arteriovenous aneurysm. Certainly, this type of headache is in every way comparable to migraine and it must be other than chance that the pain is limited to, or at least more severe on, the side of the aneurysm.

The headache in migraine results from distention largely of the extracranial and the middle meningeal arteries (9). Since these vessels have all been shown, in the previous discussion, to be abnormally large and more particularly so on the side of the lesion in cases of cerebral arteriovenous aneurysm, it is fair to assume that their dilatation is responsible for the type of pain under consideration. The presence of headache at one time and not at another probably depended upon factors influencing vascular tone in general; for example, the headaches were matutinal which is also characteristic for migraine.

Additional facts in the cases to support the analogy are present. In Case 1 the headaches were greatly improved after a decompression operation in which the middle meningeal artery necessarily was transected low in the temporal fossa. Also, several of the abnormal

communicating arteries between the aneurysm and the middle meningeal artery were severed. Since the area of the decompression gave little or no evidence of the presence of increased intracranial pressure, it is reasonable to conclude that interruption of the middle meningeal artery and its abnormal connections with the aneurysm was responsible for the relief of headache. Transection of the middle meningeal artery near the foramen spinosum in patients with migraine has served to diminish their pain until regeneration of the artery or its nerve supply permitted a return (9). The developments in Case 5 further support this belief for here the ligation of the external and internal carotid arteries on the side of the lesion served to improve the headaches greatly. On the basis of the diminution in the intensity of the bruit over the homolateral eyeball but not elsewhere over the head, the inference is that the vascularity of the branches of the external carotid was proportionately more affected than was the aneurysm itself by the combined ligation.

It is unlikely that the dilatation of the cerebral arteries, per se, plays any rôle in this migrainous headache. Normally the arteries and veins over the lateral and superior convexity of the brain are insensitive to pain when stimulated with faradic current (20) and it was found in Case 6 that stimulation of the abnormal vessels of the aneurysm in the same regions over the cortex failed to cause pain. There is still to be considered the possibility of the dilatation of the intracranial portion of the internal carotid and the proximal one to two centimeters of the mid-cerebral arteries as a contributing factor to the headache in these cases, for these vessels are normally pain sensitive in this area. The pain resulting from their stimulation, however, has a localization in and about the homolateral eye which is somewhat different from the frontotemporal pain following stimulation of the middle meningeal and temporal arteries and the location of pain in the cases under consideration was largely frontotemporal (20). Also, the pain arising from the extracranial and meningeal arteries in migraine is relieved by ergotamine (9) while it is not so certain that the pain arising from the dilatation of cerebral



arteries is relieved by this drug. In Case 5 the injection of half an ampul (.25 mgm) of ergotamine stopped the headache on the one occasion when it was tried.

The possible contribution to headache made by traction of the abnormally large superior cerebral veins upon the sagittal sinus can probably be dismissed on the grounds that the various measures mentioned as beneficial would have least effect on these veins.

Dandy's explanation for the localized headache in one of his cases was "contact of the vascular bed with the meninges." The exact mechanism he meant to imply is not clear. No part of the meninges including the pia, arachnoid and dura in this region is pain sensitive except the meningeal artery. In the case reported by Hyland and Douglas, they state "it might be possible to explain the headaches on the basis of increased blood flow transmitted to the vessels of the tumor, leading to compression and distortion of vessels in the portion of the meninges which were observed to be adherent to the tumor." Occasionally pressure upon the meningeal artery by an intracranial tumor may be sufficient to cause pain in the frontotemporoparietal region. But a more cogent explanation for the headache is the dilatation which occurs in the meningeal artery as a result of direct and indirect vascular connections with the aneurysm.

*Increased intracranial pressure and ophthalmological signs.* Increased intracranial pressure has occurred in a conspicuously low percentage of the cases of cerebral arteriovenous aneurysm that have been reported. The spinal fluid pressure was in the neighborhood of 200 millimeters of water in Cases 1 and 3 and there was fullness of the optic disks in Case 1 but none of this series had an outspoken increase in pressure. This is significant when the large size of the lesion, sufficient to distort the ventricles, is considered. The intracranial adjustment, however, begins early in life, and the changes in the aneurysm are usually gradual. It is likely that at various periods in the lives of some of these patients, perhaps following thrombosis or hemorrhage and readjustment of the aneurysm, there have been transitory periods of increased pressure.

The presence of full retinal vessels and low grade papilledema may have a different significance than is usually implied in the presence of intracranial space-occupying lesions. In the cases under discussion the total intracranial blood volume is increased and the venous pressure is high. Even though there may be sufficient readjustment of the brain to minimize or counteract sustained increased intracranial pressure, both the veins and the arteries of the eye may be enlarged. The veins enlarge due to increased venous pressure and the arteries enlarge as a part of the regional arterial dilatation discussed earlier. Associated changes in the appearance of the disk itself therefore may be the result purely of local vascular changes, such as local venous stasis. Papilledema is a common accompaniment of the venous stasis that occurs with fistulas between the carotid artery and cavernous sinus. In Case 1 there was a slight bilateral papilledema, less than one diopter, and more pronounced on side of lesion. In this case also, the retinal veins as well as the arteries were full, tortuous, and sometimes difficult to distinguish from each other. In Cases 2, 3, and 5 the retinal vessels had a similar appearance on the side of the aneurysm while in Case 4 the change was present in both eyes.

None of the 6 individuals had exophthalmos or pulsating eyeballs and this may usually be relied upon to differentiate the congenital cerebral aneurysms from the acquired fistulas of the carotid artery and cavernous sinus which characteristically cause unilateral pulsating exophthalmos. However, slight exophthalmos without pulsation of the eyeball sometimes greater on the side of the lesion has been reported in association with the cerebral aneurysms (1) and Cushing and Bailey (3) were impressed with its incidence in a third of their cases. They concluded that both the exophthalmos and the full retinal vessels were the result of "pumping arterial blood directly into the cerebral veins, a condition which is, in the nature of things, more marked in the vicinity of the lesion." Pulsating exophthalmos in connection with a cerebral arteriovenous aneurysm reported by Rotgans and Winckler was said by Cushing and Bailey (3) to be the only instance of its kind.

TABLE II.—ABNORMALITIES IN ROENTGENOGRAMS OF THE SKULL

Case No.	Side of lesion	Enlarged head	Accentuated vascularity of the skull	Enlarged grooves of middle meningeal artery	Enlarged foramen spinosum	Signs of increased intracranial pressure	Erosions—pressure of vessels of aneurysm	Intracranial calcification
1	Left	No	Both sides. Greater in front and on left	Left	Not examined	Thin posterior clinoids	Left parietal	Left fronto-parietal cortex. Left internal carotid artery
2	Right	No	Marked on both sides	Right	No change	Slight "digitation" and thin posterior clinoids	Right parietal	None
3	Right	No	Moderate on both sides	Both sides. Right > left	Right > left	Slight "digitation" and thin posterior clinoids	Right parietal	None
4	Right	Yes	Slight on both sides. Right > left	Right	No change seen (right larger at autopsy)	None	None	None
5	Left	?	Bifrontal	Both sides. Left > right	Not examined	None	Left parieto-temporal	Left parietal, subcortical
6	Right	No	Both sides. Greater in front and on right	Both sides. Right > left	No change	None	Right parietal	None

## AIDS TO DIAGNOSIS

*Spinal fluid.* Spinal fluid examination has a limited value in the diagnosis of cerebral arteriovenous aneurysms since there was nothing constant in the findings in all cases. In Cases 1 and 3 the resting pressure of the fluid was slightly elevated (in the neighborhood of 200 millimeters of water), but in only one of these was the total protein content elevated (.050 gram per cent). In Cases 5 and 6 the total protein was .040 gram per cent which is considered to be the upper limits of the normal value. In Case 4 the spinal fluid, collected shortly after the advent of spontaneous hemiparesis, failed to show any abnormalities. It should be mentioned, however, that since these aneurysms are prone to rupture, the finding of blood in the cerebrospinal fluid should always raise the question of their presence.

*Roentgenography of the skull.* A study of the roentgenograms of the skull in the 6 cases of this series resulted in the discovery that some changes due to the presence of a cerebral arteriovenous aneurysm were present in all cases (Table II). Brock and Dyke in a similar analysis of 5 cases found some distinctive changes in the roentgenograms of all. The important abnormalities in this series were: (a) Questionable or slight signs of increased intracranial pressure, present in Cases 1 and 2. (b) Increased vascularity of the skull

(enlarged diploe), present in Cases 1, 2, 3, 4, 5, and 6. (c) Enlarged channels for the middle meningeal arteries, present in Cases 1, 2, 3, 4, 5, and 6. Enlargement of the foramen spinosum, present in Case 3. (d) Local atrophy due to pressure of the aneurysm, present in Cases 1, 2, 3, 5, and 6. (e) Calcification in the vessels of the aneurysm, present in Cases 1 and 5. (f) Overgrowth of the cranium causing large head, present in Cases 4 and possibly 5.

The enlarged diploe are manifestations of the general increase in venous pressure of the region. The increased pressure in the cerebral veins and sinuses is transmitted directly to these venous channels in the skull and an example of the degree of the pressure is the force with which blood spurted from the temporal diploic vein at operation in Case 3. Most of these changes in the skull demonstrable on the roentgenogram have been mentioned by others (1, 18), but the localized, often oval shaped, areas of rarefaction due to erosion of the inner table of the skull overlying the abnormally large, pulsating vessels of the aneurysm have received little attention. These areas were present in 5 of the cases of this series and in 4 the relation of the depressions to large vessels was demonstrated at operation.

Possible enlargement of the foramen spinosum as a result of dilatation of the middle meningeal artery could not be determined

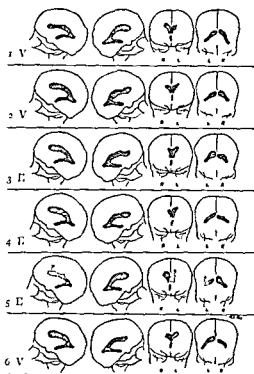


Fig 19 Composite of ventricular configurations demonstrated by injection of air in the 6 cases of this series. V, Indicates ventriculography, E, indicates encephalography. Note that there is some slight abnormality present in all cases.

from the plates in all the cases but was observed to be present in striking degree in Case 3 (see Fig. 4b). A similar finding has been reported by Lindblom. Enlargement of the cranium has not been mentioned by others as a secondary feature of the cerebral vascular malformations and it was not evident in the 4 oldest patients of this series but in the 2 children, Cases 4 and possibly 5, there was enlargement of the head. This enlargement did not appear to be the result of increased intracranial pressure but probably was a form of overgrowth comparable to that seen in the extremities in the presence of arteriovenous fistulas. Thickening of the skull occurring in 2 patients as a result of "overvascularization" was mentioned by Brock and Dyke.

**Air studies—encephalography and ventriculography** (see Fig. 19) In this series ventriculography was performed upon 3 of the pa-

tients and encephalography upon 3. In every instance there was some distortion or displacement in the ventricles although the defects were not always pronounced. The irregularity in the ventricular outline, as it occurred in Case 2, is probably due to enlarged aneurysmal vessels in the wall of the ventricle at that point and gives a clue to the depth of a lesion which appeared at operation to be largely on the surface of the brain. The distinct shift of the ventricles to the side opposite the lesion occurred in Cases 3 and 4 even in the absence of increased intracranial pressure. Scanty amounts of air appeared in the homolateral ventricle in Case 5 and while this may have been due to faulty manipulation of the head at the time of taking the roentgenogram, it may very possibly be that the ventricular lumen on that side is extensively encroached upon by enlarged vessels of the aneurysm.

Perhaps encephalography is a safer and even more advantageous procedure to employ in these cases than ventriculography. Certainly the introduction of a ventricular needle into one of the vessels of the aneurysm might lead to speedy disaster while encephalography has the advantage of sometimes showing abnormal shadows in the sulci of the region of the aneurysm as seen in Cases 4 and 5.

**Electroencephalography.** Records of the cortical electrical activity were made in Cases 3 and 4 and gross pathological waves were recorded from all parts of the cerebrum in both. The changes were greatest over the frontal areas but approximately equal on the two sides. The test was not helpful in localizing the lesion but it may be with increased experience in use of the instrument and interpretation of its records, more valuable information in these cases will be obtained.

**Cerebral angiography** Both thorotrast (thorium dioxide solution) and diodrast (10) have been used for purposes of outlining the intracranial vasculature. There has been ample warning of the danger of the use of the former (21), yet some investigators (33) hold that the radioactive material in amounts used in the cases of this series is well within the limits of theoretical safety. There were no immediate ill effects from the use of thorotrast in 3 cases and sections of the liver showing the

presence of the substance 15 months after injection disclosed no change in the adjacent cells. Diodrast, although lacking in radioactivity, has been found occasionally to produce undesirable cerebral reactions and there is probably greater danger of its producing thrombosis of the carotid or its branches. The routine use of either substance to demonstrate the more common forms of intracranial pathology is not justified but its occasional use is warranted in cases of arteriovenous aneurysm in which it is desirable to show the exact location and extent of the lesion.

Thorium was injected three times (Cases 3, 4 and 5) and 35 per cent diodrast once (Case 4) in the cases of this series. In Case 5 no shadow was obtained, perhaps because of faulty technique but possibly because of increased circulation time in the brain. Usually the radiopaque substance outlines only the cerebral vessels of the side on which the injection is performed as seen in Figure 10. But in Case 3, 8 months after the carotid arteries on the side of the aneurysm were ligated, thorotrast injected into the opposite carotid crossed over through the anterior communicating artery and outlined the lesion as shown in Figure 6. In Case 4 diodrast injected on the side opposite the aneurysm, after ligation of the homolateral carotids, was found not only to outline the normal cerebral arteries of that side but also to cross over and outline the lesion. It would be interesting to know in these cases if injection of the radiopaque material on the contralateral side would have outlined the lesion had the homolateral carotids not been occluded, for it would supply additional information about the cerebral circulation in the presence of the aneurysm.

#### THERAPEUTIC CONSIDERATIONS

The very nature of cerebral arteriovenous aneurysms makes it impossible to settle upon a completely satisfactory method of treatment. The oftentimes unhappy experiences in the use of various forms of treatment have introduced a note of caution and indeed the question has been raised whether any treatment should be attempted. Because there is the threatening possibility that persons with this lesion may die from spontaneous rupture

of one of its vessels (41 per cent quoted by Dandy), especially during a convulsion, there is an incentive to utilize whatever reasonably may offer benefit. The experience with varied treatment resulting in some benefit in symptoms in the cases of this series, has seemed to justify this attitude.

*Decompression operation combined with exploration.* This operation was performed in 4 patients (Cases 1, 2, 3, and 6). No attempt was made in any to remove or ligate the cerebral vessels of the aneurysm. However, some of the abnormal vessels that anastomosed directly with the dural (middle meningeal) arteries were transected and also the main trunk of the enlarged middle meningeal artery was interrupted low in the temporal fossa, as a part of the decompression. A moderate sized decompression beneath temporal muscle was produced even though there were no frank signs of increased intracranial pressure.

The value of this type of operative procedure is that the nature of the lesion can be positively identified; some of the arterial supply to the aneurysm through the middle meningeal artery can be eliminated; the interruption of the middle meningeal artery may be beneficial in those with local headache; the decompression relieves whatever co-existent or transitory increased intracranial pressure there may be; and subsequent roentgenotherapy may be more effectively directed at the lesion through the defect in the skull, though the latter is by no means certain.

The disadvantage and danger of an osteoplastic operation or even of a simple subtemporal decompression is the threat of serious hemorrhage, particularly from inadvertent tearing of the large vessels of the aneurysm.

*Ligation of the carotid arteries.* This procedure has been performed in Cases 3, 4, and 5 of the series. In all 3 patients the common and external carotid arteries on the side of the aneurysm were ligated and in addition, in 2 (Cases 3 and 4), the internal and external carotids on the opposite side were ligated 8 months and 15 months later.

The value of this type of operative procedure is that the arterial supply, and thus the tension, of the vessels of the aneurysm is diminished. It may be effective in lessening

the danger of spontaneous rupture and be conducive to the spontaneous occlusion of some of the vessels. The favorable effect upon the heart in minimizing the arterial supply to the lesion is well demonstrated in Case 4 (see Figs. 9a and b). An unanticipated benefit that resulted from operation was the marked improvement in headache in Case 5, the only one of these 3 with headache to begin with.

The hope, when the carotids are occluded, is that just enough arterial blood will be diverted from the lesion to accomplish the desired results but not so much that serious anoxia of the brain will ensue. Because of the extensive collateral circulation, the factor of safety in the ligation of any single artery is greater than in persons without arteriovenous communications. The ill repute of ligation of the carotids as the cause of hemiplegia and death is the result largely of ligations for infections, injury, and malignancy in the neck and face (6, 14, 18), states not at all comparable to the arteriovenous aneurysm. Watson and Silverstone report a 55 per cent mortality in 20 patients having unilateral ligation of the common carotid for carcinoma of the head and neck whereas in Matas' series of 80 occlusions of the common and internal carotids (presumably all for intracranial arteriovenous anomalies) the mortality was 7.5 per cent.

Occlusion of the common carotid alone is less dangerous but at the same time less effective in diminishing the arterial supply to the aneurysm than occlusion of the internal carotid. This is due to what has been spoken of as "reversal of blood flow" in the external carotid after ligation of the common carotid. Dorrance estimated that ligation of the common carotid alone removed but 50 per cent of the blood flow through the internal carotid. Keegan found that ligation of the common carotid alone was followed in a few weeks by enlargement of the external carotid, "necessitating later ligation of the internal carotid with more lasting benefit." For more complete effects therefore it is necessary to ligate the external or the internal carotid subsequently.

Occlusion of the internal carotid alone, because of its anatomical arrangement, is some-

times not easily or safely rectified if it is found necessary to remove the ligature on the development of late cerebral disturbance. Also, occlusion of the internal carotid alone, in an effort to diminish extensively the supply to the aneurysm, as shown in the second operation in Case 3, disregards the rich collateral supply to the aneurysm via the external carotid through numerous anastomoses (see Fig. 18). However, the lesson to be learned from the experience in Case 4 is that simultaneous ligation of the internal and external carotids carries more hazard than successive ligation with an interval sufficiently long to permit accommodation.

The frequency with which some type of reflex from the carotid sinus occurs at the time of carotid ligations is not impressive. In most normal individuals it is difficult or impossible to induce such a reflex experimentally when the region is fully exposed at operation. It has been suggested (6, 30) that ligation of the internal carotid carries additional hazard because of resulting dilatation of the carotid sinus, subsequent fall in blood pressure, and therefore even greater embarrassment to cerebral oxygenation. Doubtless this possibility deserves some consideration, but the reflex can be avoided by infiltration of procaine into the carotid sinus and furthermore the dissection associated with placing a ligature about the internal carotid is usually sufficient to interrupt the important connecting nerves of the sinus. One should perhaps be equally on the alert for the reverse action, that of marked rise in pulse and blood pressure, sometimes attending ligation of the common carotid as in Case 3. Here the temporary relaxation of the arterial wall and of the intrasinal pressure is responsible for the reflex but it too can be avoided by the local infiltration of procaine, and by the time the effects of the drug have worn off there will have been sufficient compensation for the change in intravascular pressure.

That the ligations of the carotids in these patients materially lessened the arterial supply to the aneurysms is demonstrated by the diminution in the intensity of the bruit over the head and by the marked drop in the abnormally high oxygen content in the internal

jugular vein (see Cases 3, 4, and 5). The development in Case 4 of transient hemiparesis 2 days after the first carotid ligations and in Case 5 of 3 convulsions (her first) a few weeks after ligation was probably the result of thrombosis in some of the small vessels of the aneurysm. The generalized convulsions, coma, and death following the last ligation of the carotids in Case 4 were due to acute generalized cerebral anoxia rather than to any local effects upon the vessels of the lesion.

The benefit of simultaneous ligation of the proximal vein in arteriovenous aneurysms elsewhere in the body suggests that possibly simultaneous ligation of the internal jugular vein would be of comparable benefit (22). Its purpose would be to prevent the development of inadequate intravascular tension after carotid ligation. But since the arrangement of the vascularity of the brain is not quite comparable to that anywhere else, the indications for jugular venous ligation are not so clear.

*Roentgenotherapy.* One of the hoped for developments in a cerebral arteriovenous aneurysm is the eventual obliteration of the lesion by a process of gradual thrombosis. As a possible aid to this process the administration of x-ray radiation has justification. It was used to the limit in Case 3 and nearly so in Case 2, yet there is nothing to indicate that it produced the desired effects. It might be reasoned that the effectiveness of its use would be enhanced if ligation of the carotids had been performed first. Because of this it is planned to withhold roentgenotherapy in other cases, at least until after all has been accomplished with carotid arterial ligations that can be.

Cushing and Bailey were hopeful about the benefit of roentgenotherapy, principally from the developments in 1 patient. In this case re-exposure of the lesion after prolonged irradiation disclosed its almost complete devascularization and calcification.

*Surgical attack of the cerebral lesion.* This has not yet been tried on any of the cases of this series and there is little in theory or in others' experience with such attempts to recommend it. The most obvious argument against it, at least as far as the aneurysms involving the mid-cerebral artery are concerned, is that the blood supply to the motor

cortex would most likely be destroyed if a radical excision or ligation of the proximal portion of the artery were attempted. Anything less than this, such as ligation of some of the vessels of the aneurysm, might serve to make the aneurysmal condition worse. Thus, the radical attack upon the lesions seems to be indicated only when hemorrhage threatens the patient's life.

In case the lesion should become inactivated by thrombosis of its vessels it might then be removed with greater safety. But if the indication for such a procedure should be convulsions alone, one should, as Dandy aptly points out, appreciate that there is no assurance of a permanent cure of epilepsy even after the cure of an aneurysm.

In an additional patient with a left cerebral arteriovenous aneurysm encountered since this paper was submitted for publication, a craniotomy was performed and the walls of many of the aneurysmal vessels on the surface of the brain were coagulated with the electrosurgical unit. The caliber of all the vessels treated in this manner was greatly diminished but few vessels became completely occluded. The procedure was followed by hemiparesis and aphasia from which there was slow but nearly complete recovery. The bruit was unaffected.

This method of treatment was suggested by Horrax<sup>1</sup> and deserves further trial in selected cases.

In résumé it may be said that the prognosis in individuals with cerebral arteriovenous aneurysms is not encouraging. All the methods of therapy discussed here leave much to be desired. But there is some merit in all of them, alone or in combination, and they can be used to advantage to suit the individual problem that each case presents.

#### SUMMARY AND CONCLUSIONS

1. Observations on 6 patients having cerebral arteriovenous aneurysms substantiate the conclusion that these lesions are congenital and can be identified both by the clinical signs and symptoms they produce and by their appearance when exposed at the operating table.

<sup>1</sup>Horrax, G. A two to eight year follow up study of 215 cases of benign brain tumor with special reference to the uncommon varieties. *Tr. Am. Neurol. Ass.*, 1941.

2. A bruit heard on auscultation over some part of the head, the eyeballs, and the carotid arteries in the neck, is a characteristic sign. This, in conjunction with Jacksonian convulsions or unilateral motor and sensory disturbances, is usually sufficient to permit a diagnosis to be made.

3. Changes in the skull that may be shown on roentgenogram include slight signs of increased intracranial pressure; increased vascularity of the skull; deepening of the grooves for the middle meningeal arteries; local atrophy of the inner table from direct pressure of the vessels of the aneurysm; enlargement of the head; and calcification in the lesion.

4. Air studies may be relied upon, in many instances, to demonstrate abnormalities in the ventricles and subarachnoid spaces. Encephalography in such cases is safer than ventriculography.

5. Cerebral angiography is indicated in order to visualize the extent and the location of the lesion.

6. The collateral circulation is extensive. It involves anastomosis between the external and internal carotid arterial systems, principally through the orbit and through the meninges.

7. The effects of the aneurysm upon the general cardiovascular system are variable but not necessarily serious.

8. Headache, localized on the side of the lesion, is usually due to pain arising in the dilated arteries, chiefly in branches of the external carotid artery.

9. Reasonably safe methods of treatment include exploratory osteoplastic operation and decompression, successive ligation of the carotid arteries in the neck, roentgenotherapy. None can be relied upon to be curative but used alone or in combination they may be beneficial.

10. Ligation of carotid arteries is safer in individuals with cerebral arteriovenous aneurysms than in others because of the rich collateral circulation.

11. Direct operative attack upon the lesions is dangerous but might be indicated in selected cases.

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# THE SURGICAL TREATMENT OF ACUTE CHOLECYSTITIS IN PATIENTS FIFTY YEARS OF AGE AND OVER

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A NOTABLE advance in surgery in recent decades has been its application to patients of advanced years, for, at the beginning of the century, such patients were subjected to surgery only as a last resort. The medical literature today is granting an increased consideration to the question of lessening the risk of operation in patients over 50 years of age, for it is recognized that they form a large group, urgently needing surgery but accounting for many of its failures. The more intelligent preoperative treatment, safer anesthesia, and greater attention to operative details have removed many of the hazards of operation in older patients. In the surgical treatment of acute cholecystitis there persist two problems: one is the change in the biliary tract, the result of prolonged infection; the other, the systemic disorders common in advanced age. Acute cholecystitis in a patient over 50 years of age rarely is a simple acute inflammation in a formerly healthy gall bladder but is an exacerbation of a long standing chronic disease which may have damaged the entire biliary tract. The general systemic disturbances are vascular, such as arteriosclerosis, nephrosclerosis, cardiac disease, and hypertension. There is evidence for believing that there is an interaction between these conditions, or at least an unfavorable reaction of the organisms as a whole to long standing biliary disease, for the incidence of organic disorders, in our experience, is higher in patients with, than in those without, disease of the gall bladder. The patient 50 years of age or more who is admitted for surgical treatment of acute cholecystitis is, therefore, likely to be one whose biliary tract has been damaged and whose general systemic status shows signs of age beyond his years. For these, it is imperative that every precaution be taken to avoid com-

plications following surgery. This obligates the surgeon to evaluate the risk in the individual case by every possible means and to combat, before operation, the manifestations of general systemic disturbances.

Over a period of 7 years at the New York Hospital we have treated surgically 1,102 patients with nonmalignant disease of the biliary tract. In this group there were 267 patients suffering from acute cholecystitis and 835 with chronic biliary tract disease. The total number of patients 50 years of age and over was 276. There were 93 patients 50 years of age and over who had acute cholecystitis. It is with these patients that we are herein concerned.

The eldest patient was 75, and the average age for the 93 was 56.6 years. There were 64 women and 29 men. In seeking to estimate the duration of symptoms one is impressed with the difficulty with which adequate histories are obtained. If one is persistent the history is readily extended into the early decades. Intolerance to fatty foods, indigestion, belching accompanied at intervals with pain, nausea and vomiting, rarely accompanied by jaundice, constituted the frequent history. From a few patients a history of frank biliary tract disease of 30 to 40 years' duration was obtained. While it is true that some of the patients were too ill to permit the obtaining of a satisfactory history, it is highly improbable that the primary disease was of recent origin in any instance. The duration of the attack resulting in the hospitalization of the patient varied from a few hours to 10 days with an average time interval of 18 to 24 hours. That stones were present in the gall bladder or biliary passages of each of the 93 patients is additional evidence in favor of a process of long standing. In a review of over 1,100 patients with biliary tract disease we have found that the most complete histories place the onset of symptoms in women in the



twenties and early thirties, very often associated with the first or second pregnancy. In nulliparous women and in men it seemingly is about a decade later. The common dictum that gall-bladder disease is limited to the "fair, fat and forty" is only a partial truth.

In these patients 50 years of age and over, the surgeon is concerned not only with the biliary tract disease but with general systemic disorders as well. The incidence of systemic disturbance before operation was as follows: hypertension (diastolic over 90), 42 cases, or 45 per cent; arteriosclerosis, 47 cases, 50 per cent; cardiac disease, 38 cases, 40 per cent; diabetes, 10 cases, 10 per cent; renal disease, 8 cases, 8 per cent. By the term hypertension we refer to a diastolic pressure of 90 and over. Cardiac disease was indicated by cardiac enlargement as shown by roentgenograms, or coronary disease as evidenced by electrocardiographic changes. The diagnosis of diabetes was based on glycosuria and an elevated blood sugar. The diabetes was, for the most part, of a mild nature requiring only diet regulation after recovery from the acute illness. Two, however, were severe enough to require fairly large dosages of insulin. Impaired kidney function as determined by urine concentration, urea clearance, and the persistence of an albuminuria following recovery from the acute illness was found in 8 patients. It has been our experience that albuminuria, elevated urea nitrogen, and the presence of blood cells in the urine during the acute illness often disappear as the patient's condition improves. The occurrences of these disturbances is of much higher incidence than in a similar age group without biliary tract disease.

#### OPERATIVE PROCEDURES

The procedure of cholecystostomy was performed in 16 instances. Four deaths followed. This operation is clearly indicated under certain circumstances; as when the patient is too ill to withstand cholecystectomy, or when cholecystectomy presents too great difficulties. For the extremely debilitated patient or for the very ill, we doubt if there are any contraindications for cholecystostomy because it may be done under local anesthesia, disturbing the patient very little. Such an operation may

be a lifesaving procedure. It decompresses the biliary tract and averts catastrophe by preventing progressive liver damage if complete biliary obstruction is present. In this group of 16 patients who were treated by cholecystostomy it appears to us that the conservative procedure was responsible for the recovery of the very ill patients. The 4 who died were in such straits that it is very likely that they would have died regardless of whether or not they were operated upon, and furthermore, regardless of the type of operation. Five of these patients later had cholecystectomy performed. Four were uncomplicated; 1 at operation was found to have a fistula between the lower portion of the gall bladder and the duodenum. All made an uneventful recovery.

Cholecystectomy was carried out in 69 patients with 2 deaths. This, when feasible in the opinion of the surgeon, is the operation of choice because it removes the primary site of the disease as well as the principle source of acute complications. Generally speaking, the acutely inflamed gall bladder is removed with ease. However, in this group of patients cholecystectomy may be difficult. It should be done with care, subjecting the liver to a minimal amount of trauma.

Common duct exploration in acute cholecystitis has been limited by us to the same indications as in chronic biliary tract disease. If it is indicated the duct should be explored and stones removed. The incidence of post-operative complications was not apparently increased by this procedure in this series. Twelve patients were subjected to common duct exploration—stones were present in 6, or 50 per cent. It would seem that the urgency of the situation when a stone is in the common duct outweighs the hazards of the procedure. Decompression, i. e., cholecystostomy, may be utilized as a compromise procedure, the plan being to explore the common duct at a later date when the patient's condition has improved. In this group of patients only 1 such case was encountered.

At operation there were found 64 instances of acute cholecystitis, 18 instances of acute cholecystitis with gangrene, and 11 instances of acute cholecystitis with gangrene and per-

TABLE I.—SUMMARY OF DEATHS AFTER OPERATION

History number	Sex	Age	History of biliary disease	Duration of attack	Jaundice	Findings	Operation	Cause of death
1. 51,896	F	66	8+ yrs.	3 days	+	Acute cholecystitis with perforation. Peritonitis	Cholecystostomy, drainage	Peritonitis
2. 155,437	F	67	4+ yrs.	7 days	o	Acute cholecystitis with gangrene	Cholecystostomy	Peritonitis, bacteriemia
3. 221,902	F	50	20+ yrs.	10 days	+	Acute cholecystitis, cholelithiasis, common duct obstruction	Cholecystostomy	Bacteriemia, stone in the common duct, thrombosis of hepatic artery
4. 182,841	M	72	7+ yrs.	8 days	+	Acute cholecystitis, cholelithiasis	Cholecystostomy	Liver failure, biliary cirrhosis
5. 134,502	F	57	inadequate history	4 days	o	Acute cholecystitis, cholelithiasis	Cholecystectomy, drainage of abscess	?Subhepatic abscess *
6. 59,204	F	70	12+ yrs.	8 hours	o	Acute cholecystitis, cholelithiasis	Cholecystectomy	Coronary occlusion, cardiac failure

\*No Autopsy.

foration. In determining the type of operation to be done, the gross appearance of the presenting pathological changes is of importance. In the first place, if there is gangrene and perforation with an accompanying generalized peritonitis, we recommend simple drainage of the abdomen together with cholecystostomy. If there is gangrene and perforation which has resulted in a localized peritonitis or abscess in the region of the extrahepatic portion of the gall bladder, then one may choose between cholecystectomy and cholecystostomy. However, in the presence of extensive adhesions of the omentum to the gall bladder and into the biliary fossa it is indeed questionable whether these should be disturbed and a cholecystectomy done. If the patient is unusually ill and if postoperative complications appear in the offing, then certainly cholecystectomy should not be attempted. Perforation of the gall bladder with a small abscess or perforation into adjacent liver tissue is no contraindication to cholecystectomy. The patients with simple acute cholecystitis are, in general, best treated by cholecystectomy.

In the summary of this series of patients who were treated surgically for acute cholecystitis the following facts emerge: first, biliary tract disease had been present for many years, and second, vascular changes commonly associated with age occurred far more frequently than in a comparable group without biliary tract disease. As to the first, we

were concerned about the duration of the biliary tract disease since its beginning as well as with the present acute episode. Frequently the attack which brought the patient to the hospital differed from many previous attacks only in severity and failure to subside. The significance of this failure to subside is seen in the deaths; 4 of the 6 had been acutely ill for 4 to 10 days (Table I).

A careful investigation and evaluation of each system was made in these patients. The most frequent finding was dehydration and we believe a depletion of chlorides and glucose. Parenteral glucose and saline readily correct these deficiencies. Cardiac failure, when present, impending, or anticipated, has been combatted by immediate and rapid digitalization without cause for regret so far. Sometimes cardiac and biliary symptoms are indistinguishable in these patients. Support to the cardiac mechanism in doubtful cases is not withheld.

The presence of jaundice requires determinations of blood prothrombin and the bleeding tendency, and may indicate blood transfusions, bile salts, and vitamin K. Sulfonamide drugs should be given if a bacteriemia is discovered.

*Anesthesia.* The selection of anesthesia depends on the condition of the patient and requires judgment because many postoperative complications are attributed to it. Local anesthesia may often be used to advantage for limited procedures such as cholecystos-

tomy and also for the beginning of an operation, general anesthesia being substituted if a greater procedure is decided upon. Our experience thus far leads us to believe that open drop ether is the safest general anesthesia for these patients. First of all, it is satisfactory from the standpoint of relaxation allowing an adequate exposure and aiding thereby to the ease with which the operation can be done; and, secondly, in our hands, the incidence of postoperative pulmonary complications is less than in those patients who had other types of anesthesia.

The distribution of anesthesia in the series was as follows: local in 12 patients; spinal in 2; ether in 32; ether in combination in 10; ethylene in 19; cyclopropane in 18.

*Postoperative complications.* These are grouped for convenience into pulmonary, cardiac, wound, and miscellaneous complications.

There were 4 pneumonias, 2 of which were bronchopneumonias, 1 following local anesthesia, 1 following cyclopropane. Lobar pneumonia occurred in 2 patients after open drop ether anesthesia. All recovered without residual complications. Pulmonary infarction occurred twice, one associated with a phlebitis of the leg. Two patients had atelectasis of the right lower lobe which was discovered early and cleared without prolonging the patients' hospital stay; both of these were following open drop ether anesthesia. These patients ranged in age from 50 to 65. The incidence of postoperative pulmonary complications is only slightly higher than for patients under 50 years of age.

Pulmonary edema followed auricular fibrillation in 1 instance, but the patient recovered after digitalization. Auricular fibrillation was not considered a postoperative complication unless accompanied by some manifestation of cardiac failure. In 3 patients there occurred cardiac failure sufficient to produce dependent edema which cleared as the patients' condition improved or as digitalization was completed.

There were 2 instances of wound dehiscence. In one there was gross infection of the wound, in the other cultures taken were negative for bacterial growth. It was ascribed to postoperative hiccupping and vomiting. The

wounds were resutured with through-and-through silver wire. Four wounds were superficially infected and 3 showed infection extending down to and involving the fascia. There were 2 hematomas, one occurring in a jaundiced patient and another in a non-jaundiced patient who had cirrhosis of the liver.

Two patients following operation were found to have a positive blood culture, 1 due to colon bacilli and 1 due to *Bacillus lactis aerogenes*. The same organism was obtained from the peritoneal cavity at the time of operation and blood cultures became negative as the clinical condition improved. Three patients developed phlebitis of the lower extremities without accompanying pulmonary emboli.

The average age of the 6 patients who died was 63.6 years. All but 1 were found to have had unmistakable symptoms of gall-bladder disease for years. The duration of the attacks, with 1 exception, was prolonged over a period of days before admission to the hospital. Jaundice was present in 3 of the 6 patients. The findings at operation included those complications which take place in acute cholecystitis, namely, gangrene with perforation, abscess formation, peritonitis, common duct obstruction, and bacteremia. There was only 1 instance of uncomplicated acute cholecystitis in the 6 deaths, and death in this patient was due to coronary occlusion.

The expectancy of life at birth has been almost doubled during the past half century in the United States (3). Our general population is, therefore, becoming one with a greater percentage over 50 years of age. The surgical therapy accorded these people is on the increase. And although malignant disease is the most common ailment requiring surgery in the later decades, biliary tract disease is by no means rare, as is evidenced by the foregoing résumé. Surgery in the early phases of biliary tract disease should be looked upon not only as an immediate therapeutic measure but also as a preventive one. We have observed in our own series of cases that the mortality in the treatment of gall-bladder disease increases with the age of the patient. In 826 patients under 50 years of age the post-

operative mortality was 1.0 per cent; in 186 patients from 50 to 59 years of age was 7.5 per cent; in 77 patients from 60 to 69 years of age was 13 per cent; in 13 patients of 70 or more years, 30 per cent. For 93 patients with acute cholecystitis, 50 years of age and over, the mortality was 6.4 per cent.

The data collected in our experience suggest that the changes in the vascular system, i.e., arteriosclerosis, hypertension, etc., are greater in these 93 patients than in a corresponding number without biliary tract disease. Cowdry (1) in a volume on arteriosclerosis places the incidence of arteriosclerosis in the general population at 25.6 per cent for those between 50 and 60, and 38 per cent for those over 60. McCallum (2) found that patients over 50, dying as a result of gall-stone disease in the Johns Hopkins Hospital, showed an incidence of arteriosclerosis in 68 per cent.

The surgical treatment of biliary disease and its complications makes up only a part of the surgery of geriatrics. This small series of 93 patients with acute cholecystitis represents rather well a common problem today. They should be regarded with great care. Preventive surgery should reduce their number, i.e., the surgical treatment of biliary tract disease in the earlier decades when acute cholecystitis represents an early phase of the disease. If our contention is correct, a deleterious effect upon the vascular system may be interrupted.

#### CONCLUSIONS

1. Acute cholecystitis occurs frequently enough in patients over 50 years of age to warrant special consideration by physician and surgeon.

2. In this group of patients acute cholecystitis may well be looked upon as a complication of a disease of long standing.

3. The incidence of organic disorders, and in particular those of the vascular system, is higher in patients with, than in those without, biliary tract disease.

4. Acute cholecystitis in patients over 50 years of age requires urgent surgical consideration.

5. The trend of our population toward the older age groups indicates that we may anticipate an increasing number of these geriatric problems in the practice of surgery.

6. The recognition of the extent of the clinical problem involved in the care of these patients, the employment of adequate but conservative surgical therapy, and the according of proper attention to the vascular system should contribute to a further reduction of the mortality rate.

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# CONGENITAL CLEFTS OF THE FACE AND JAWS

## A Report of the Operations Used and a Discussion of the Results

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IN a chapter bearing the same title as this article (5), the writer has detailed a voyage of discovery made through many channels of interest in an urgent effort to find an answer to the question "What should be done?" to reconstruct the deformity and prepare the baby for future growth and development. Based on the findings in the embryology, anatomy, and physiology of the tissue involved, some suggestions were made on the technical steps of operations, and the reasons for them were stated. The steps of procedure were illustrated by diagrams. In 1936, I had an opportunity of revising the chapter, in order to withdraw statements and illustrations made on the use of direct force applied to the upper jaw, which I did because of my experience in the use of wire and plates. Such distressing results followed their use, with malocclusion and long years of orthodontia, that in some cases the surgical deformity seemed worse than the embryonal deformity, so I could not allow the plans to remain permanently in the literature. Since that revision, and particularly since the first printing, many notable papers have appeared in the literature suggesting new plans, and modifications of combinations of old ones, offered by men of wide experience, so many that I felt that they should be discussed in relation to the propositions made in the chapter. Most of the more recent papers have to do with the palate. The dental surgeons are also entering the list of contributors, to indicate that what we have been doing to the hard palate interferes with the normal development of the upper jaw. This is a most important observation, because it is the late results which are the most important, and it is up to us who do the primary repair to take cognizance of these reports. I thought that, instead of merely discussing these new plans, I would show a series of cases, tell what was done to them, locate the newer

suggestions, discuss more fully the age for, and sequence of, operation and frankly criticize the results of my operative efforts. The cases are shown in the order of the classification and plan of record, the whole story of the development of which has been covered in my contribution to *Practice of Surgery* (5).

### GROUP I. PREALVEOLAR PROCESS CLEFT. THE GROUP I CASES

Dr. Sherman's descriptive term is used for those cases in which the deformity is in front of a normal process and therefore is one of a lip problem only. Four cases are here shown to illustrate common degrees, with the caution that really no 2 cases may be exactly alike, and that in between these 4 cases there are those which merge from one degree into another. This deformity has been described as a simple harelip. The term "incomplete harelip" is also applied because there is never a cleft in the floor of the nostril, although, as in Figure 4, the ala may show some distortion. These cases, however, constitute a most important group, because the lip cleft is the only cleft present and thus can be subjected to the closest study. It was the clinical observation of these cases which led to the anatomical and physiological study of the tissues involved, which in turn led to the conclusion that the various forms and degrees of any cleft lip were readily explained by the position and disposition of the muscle elements in each case. The muscle theory repair of the lip was presented in 1928 and has been elaborated in the chapter in *Practice of Surgery*. It was an effort on my part to find some index to lead me to a proper repair of the lip which would substitute any personal opinion as to how it should be done, and would be something that would fit any lip. Review these cases carefully, as I believe that the conclusions are obvious and are fundamental to repair of any lip cleft.

**Lip Column**



**Draw in Degree**

**SPECIAL EXAMINATION**

**Process and  
Palate Column**

**GROUP I. PRE-ALVEOLAR (Process) CLEFT. (Lip cleft. Process normal).**

- Unilateral. Right } Complete (Cleft extends into nostril) \_\_\_\_\_  
 Left } Incomplete (Does not extend into nostril) \_\_\_\_\_  
 Left } Complete \_\_\_\_\_  
 Left } Incomplete \_\_\_\_\_
- Median (rare) Complete \_\_\_\_\_ Incomplete \_\_\_\_\_
- Bilateral. Right } Complete \_\_\_\_\_ Left } Complete \_\_\_\_\_  
 Left } Incomplete \_\_\_\_\_ Left } Incomplete \_\_\_\_\_

Describe nostrils \_\_\_\_\_  
 NOTE: If associated with palate cleft, also fill in GROUP II form.

**GROUP II. POST-ALVEOLAR (Process) CLEFT. (Palate cleft. Process normal).**

- Soft Palate \_\_\_\_\_ Extent in thirds \_\_\_\_\_
- Hard Palate \_\_\_\_\_ Extent in thirds \_\_\_\_\_
- Situation and attachment of septum \_\_\_\_\_
- Measurement of widest portion of cleft \_\_\_\_\_
- Palatine Arch \_\_\_\_\_ High \_\_\_\_\_ Low \_\_\_\_\_

NOTE: If associated with lip cleft, fill in GROUP I form.

**GROUP III. ALVEOLAR (Process) CLEFT. (Follows incisor sutures).**

- Unilateral.
 

PROCESS. Right } Complete (Cleft extends through alveolar process) _____	Left } Complete _____	
Left } Incomplete (Cleft does not extend entirely through process) _____	Left } Incomplete _____	

PALATE. Unilateral _____	Bilateral _____	Normal _____
Complete _____	Incomplete _____	
Palatine arch _____	High _____	Low _____

LIP. Unilateral _____	Bilateral _____	Median _____
Complete _____	Incomplete _____	
- Median (rare). Complete \_\_\_\_\_ Incomplete \_\_\_\_\_
- Bilateral.
 

PROCESS. Right } Complete _____	Left } Complete _____	
Left } Incomplete _____	Left } Incomplete _____	

PALATE. Right } Complete _____	Left } Complete _____	Normal _____
Left } Incomplete _____	Left } Incomplete _____	
Palatine arch _____	High _____	Low _____

LIP. Right } Complete _____	Left } Complete _____	
Left } Incomplete _____	Left } Incomplete _____	

Locate any rudimentary structure \_\_\_\_\_  
 Note projection of premaxilla \_\_\_\_\_  
 Note rotation of premaxilla \_\_\_\_\_  
 Situation and attachment of nasal septum \_\_\_\_\_  
 Measurement of cleft at alveolar process \_\_\_\_\_  
 Measurement of widest portion of palate cleft \_\_\_\_\_

If previous operations performed elsewhere, give dates.  
 Fill in original condition on proper group form.

Impression \_\_\_\_\_  
 Recommendation \_\_\_\_\_

Photographs. Date _____	No. _____	
Date _____	No. _____	
X-ray plates. Date _____	No. _____	
Date _____	No. _____	
Palate casts. Date _____	No. _____	
Phonographic speech records. Date _____	No. _____	
Date _____	No. _____	



**Draw in Degree**



**Measure Process Cleft  
Measure Palate Cleft  
Draw in Degree**



**Measure Process Cleft  
Measure Palate Cleft  
Draw in Degree**



**Measure Process Cleft  
Measure Palate Cleft  
Draw in Degree**

Fig. 1. The reverse side of the record chart is reprinted for the convenience of the reader who may not be familiar with the terms of the description of the cases which are recorded, not as harelip and palate cases but as a series of congenital clefts of the face and jaws. The clefts are grouped on the alveolar process as to the position of the clefts in relation to a normal or a cleft alveolar process, thus developing a name for the case as a whole, to indicate the position and combination of the clefts present in that case. The arrangement of the diagrams and literal translation between them was made by Dr. John Staige Davis. In 16 years of use but one change from the original has been made. In the "Group III, Alveolar (process) Cleft" cases, in both the unilateral and bilateral combination, about 10 to 12 per cent of the cases have a normal hard and soft palate, so the word "normal" has been inserted in the palate description.



Fig 2a



Fig 2b



Fig 2c



Fig 3a



Fig 3b

Fig 2 a. The case with a mere marking of the lip is usually advised against operation, as that case presents a minimal cosmetic deformity with no dysfunction. But when the line is depressed or becomes increased in depth on motion, the deformity should be corrected, because if the explanation of the defect is accepted, there is every expectation that the deformity will increase in degree on growth of the child. With the embryology, anatomy, and physiology of the lip tissues in mind, it can fairly be said that in this case the condition is due to the fact that the superficial strata of the muscle bundles in the body of the lip have failed to complete their migration and thus do not interdigitate with their fellows on the opposite side, but instead are attached to the skin and when contraction occurs the line is depressed. Of course, it is not surgically possible to identify the muscle elements, but they can at least be apposed in the line or curve of their action. Freehand incisions made on each side of the skin cleft and removal of the skin involved exposes the body of the lip. Interrupted sutures are inserted on one side at a time, deep enough to include the exposed body. If the exposed bundles are found to be contracted under the skin, they are defined by gentle under-cutting of the skin sufficiently to include them in the stitch and are pulled out with a hook to insure their inclusion in the bite of the stitch. Such a procedure offends a fundamental principle in wound suture, viz., layer series suture of the tissues, but it is done here because I believe buried sutures in the body of the lip should not be used. This opinion may be modified in the future, because there are several materials now being presented as nonirritating, but I can state from experience that buried catgut may be a cause of later trouble. This case is offered as a model for the repair

of any lip, as it illustrates the normal formation of the lip, and all I did was to complete the job by a simple surgical procedure. Great care must be taken in the exact placing of the stitch at the mucocutaneous vermillion border (see Case 2). b, Shows a voluntary contraction, outlining clearly the musculature of the lip, and points of denudation are definitely made. Please note the V-shaped depression in the lip at the base of the nostril. The same picture can be obtained by electrical stimulation while the baby is asleep. c, Please note the line of the vermillion border, the oblique direction of the suture line, the eversion of the lip, which is quite similar to the lower lip.

Fig 3 Group I. Prealveolar process cleft. Right incomplete.

In this case there is no marking on the lip except a notch at the vermillion border, which means that the superficial strata of the orbicularis oris have interdigitated, but the bundles in the body of the lip and under the mucous membrane are apart, causing a thin lip at this point without much cosmetic deformity, but with definite dysfunction of the lip. The ends of the bundles can be denuded from the mucous membrane side but the approach and suture are awkward. It requires a bit of surgical courage to break the lip down and pay the penalty of a skin scar, but since precision is a prime principle, this was done. When the body of the lip is thus denuded it is possible to put the muscle stitches in from the mucous membrane side and thus exclude possible stitch marks. By so doing the deep stitches can be removed and this excludes any worry about buried stitches. This case illustrates the care necessary in suturing the vermillion border. Note the outlines of the prolabium of the embryonal frontonasal process in photograph at left and its postoperative aspect in photograph at right.

Fig 4. Group I. Prealveolar process cleft. Left incomplete. a, The description of this case must be written in on the chart, to describe the fact that the cleft is incomplete above and complete in the lower two-thirds, and a drawing made on the diagram. While cases as in Figures 2 and 3 are not so common, this degree is most frequent. It is not my intention to repeat aforementioned studies and conclusions, but in looking at this picture, the temptation to analyze the conditions here present is too great to resist. In the lower two-thirds of the left side of the lip, the skin, body, and mucous membrane are entirely apart. In the upper third the skin and mucous membrane have contacted, but the body of the lip is thinner than normal, a condition similar to that in Figure 2. The nostril is flatter than that on the right side. The aspect of the right nostril and right side of



Fig. 4a.

Fig. 4b.

the lip is that of a normal lip. This is explained by the fact that the muscle elements on the right side have migrated from their origin in the platysma, up the soft tissues of the right maxillary embryonal process, proceeded through the prolabium of the frontonasal process and appear at the cleft margin in position to interdigitate with the fellows of the maxillary process which is out of contact. The outlines of the skin of the prolabium, which, of course, has a different origin from that of the sides, can readily be made out, with a normal vermillion border on the right, while at the cleft margin it is indicated by an obtuse angle. The tissue on each side of the cleft appears equal in length and bulk, and the obvious thing to do is to denude the bodies of the lip and sew them together as they lie, the same problem as in Figure 1. b, There is a margin of personal interpretation of the result of electrical stimulation. On the combination side it is constantly evident. On the side out of contact the bundles often appear bunched and the lower point of contracture not so definite, particularly if the tissues have been handled and because the immature muscle bundles tire quickly. When uncertain the tendency is to ink a mark too close to the cleft, and an angle appears in the vermillion border, as in this case. The angle is entirely superficial, but a result of more severe degree may give still a picture of cleft lip at this point. On the contrary, if the denudation is made too far out and the muscle stitches not precisely and symmetrically placed, the side out of contact is displaced downward and a staggered lip repair is obtained. Such results are purely technical failures and have nothing to do with surgical principles of the cleft lip operation, because in

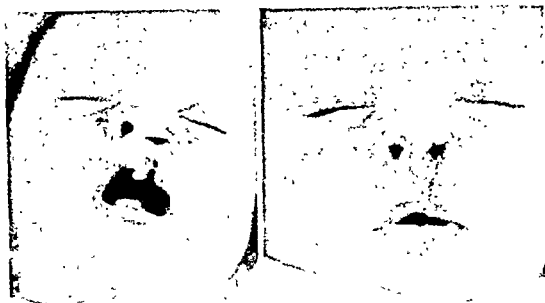


Fig. 5a.

Fig. 5b.

this case it is evident that the body of the lip has healed, and the right and left facial expression groups have been co-ordinated.

Fig. 5. Group I. Prealveolar process cleft. Left incomplete. a, This degree has been described as incomplete—a simple harelip—but with the muscle theory in mind it is a complete cleft, as there is no muscle contact anywhere along the line. This form of lip cleft is historically interesting, because it is the model upon which are drawn the lines of incision of the original Mirault operation. When I was groping around, trying to follow set operations, I noted that, with this operation, the best looking nostrils were obtained, and I never knew why, but the reason now is readily explained by the fact that the curved sweep of the upper part of the incision would denude the upper bundles of the orbicularis oris, remove the overlying epithelial tissue, and thus accomplish empirically what I have gone to such lengths to prove is a necessary step in the repair of the deformity. The technical steps in the repair of this lip are briefly repeated: The demonstration of the position of the active tissue, symmetrical denudation and suture side to side as in Figure 1, taking cognizance of the principle of layer series suture by placing the deep stitches from the mucous membrane side to include the muscle bundles and out fold the mucous membrane, which, with interrupted stitches in the skin, sutures three kinds of tissue with only two forms of stitch and thus meets the fundamental principle in wound repair. b, The only difference between this lip and the complicated picture of the group III lip is in the matter of degree, due to conditions outside of the lip itself.

## GROUP II. POSTALVEOLAR PROCESS CLEFT THE GROUP II CASES

This is Dr. Sherman's term of description for the case in which the deformity is behind a normal process. The incidence is somewhat confused, because this condition may come in for correction at any time of life, whereas in the group I and group III cases, the deformity is readily apparent, and advice is sought at, or soon after, birth. Approximately one case in five can be accepted as almost right. This case has been described as an incomplete or simple cleft palate, because the alveolar process is normally formed, but it is a cleft palate case. A great part of the literature is composed of discussion

of the relative merits of various technical procedures called cleft palate operations, which are, it seems to me, presented without regard to the form, degree, or association with other clefts which may be present in the case.

The group II cleft palate has been brought into the limelight in the past few years by Dr. George Dorrance of Philadelphia, who offered the push back operation, which was based on the belief that postoperative speech defect was due to a short palate, and that this defect could be overcome by raising the hard palate tissues in the form of a delayed flap, at one sitting, and then later attaching the forward margin of the mucoperiosteal flap to the hori-





Fig 6a.

Fig 6b

Fig 6. Group II. Postalveolar process cleft. Soft palate only. a. There is no formal diagram for this degree and the description must be written and drawn in. The condition appears only occasionally and is usually overlooked or considered so minimal that no particular attention is paid until the patient develops a speech defect. The apparent deformity is that of a uvula cleft which in itself is of no consequence, but the presence of a cleft uvula may be and usually is an index that the muscle bodies of the soft palate are apart in various degrees, up to complete failure of contact, causing a transparent soft palate, the so called submucous cleft palate. It requires some courage to break the palate down, find the muscles, and make a formal repair. This was done and the postoperative improvement in speech in this case was remarked by the whole hospital. This condition in the soft palate is comparable to that in Fig. 3 a in the lip, i. e., failure of complete muscle contact. b. The superficial stitches come out in the food and it is only necessary to remove the deep stitches about the fifth or sixth day. The soft palate at rest hangs down at an appreciable distance from the pharynx. The space can only be contracted by muscle action. The ability of this boy to speak depends upon the proper union of the two halves and whether the muscles of the soft palate are hooked up with the superior constrictor of the throat. If they are not united then he will have a curtain soft palate, without action or function.

zontal plate of the palate bone, thus bringing the soft palate into contact with the pharyngeal wall. Barrett Brown, of St Louis, has followed up this procedure with several further technical suggestions. My difficulty has been in selecting the case and deciding to do the operation, for the reason that I have not accepted the plans as primary procedures, because over many years of observation I think I have obtained equal results by much simpler operations, paying particular attention to the severing of the soft palate from the bone and to the suture of the musculature of the soft palate. In discussing the cleft palate operations, I have selected four primary case conditions to show that, because the process is closed, there is always a picture of a median cleft, which clinically supports the embryological fact that the hard palate is formed from the sides, and that the median process which is so important in the process and the lip is not

a part of the hard palate. All cases in this group have the same form of median cleft, with equal tissues on each side. One case differs from another in involvement anteroposteriorly, and this runs from a cleft in the uvula to the anterior palatine foramen. Look at Figures 6, 7, 8, 9, and 10. They are all median clefts. The obvious thing to do is to move the tissues to the midline and sew them together. The pioneers recognized this and there has come down to us an operation which is now classical, called the Langenbeck or Warren Langenbeck. This, of course, is simply a lateral sliding flap of the mucoperiosteum of the hard palate, mesially sutured, plus the median suture of the soft palate. Objections to the operation on the hard palate have long been recognized and these objections have been used in support of the many substitute operations which have been offered. Even Dr. Brophy used the sometimes necessary lateral incisions to the support of his compression methods applied to the upper jaw, although I have failed to see any suggestion of the compression methods being used in the group II cases.

Professor Veau, the master French surgeon, discussing the "division palatine," succinctly states his objections to be that the elevation and suture of the mucoperiosteal flaps leaves a blind space between the flap and the bone for the accumulation of blood clots and nasal discharge, with a chance of infection and scar formation, and that lateral incisions do not always heal and may heal by scar formation. This is an objection made by the dental surgeons, with which I heartily agree, but I wish to add one objection which is the most important of all. The classical Warren Langenbeck operation is just too much surgery to be done at one time. It was based on the whole palate theory and failed to recognize that it constituted two operations dealing with tissues entirely divorced in anatomical structure and function. Almost all of the operations deal with the hard palate, and there has been so little said about the soft palate. Professor Veau has recognized the importance of the tensor palati by his submucous wire placed to include it. Wardill has made a beautiful anatomical study to show the contact of this mus-



Fig. 7a.

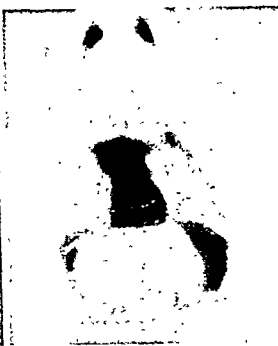


Fig. 7b.



Fig. 7c.



Fig. 7d.

Fig. 7. Group II, 1/3. This degree is most important, and I propose to relate in detail my experience in the care of this case, because so many points are brought up which are so often discussed in the literature: (1) The incidence is high. (2) I have found that in many cases the cleft in the bone is further forward than appears in the soft parts. (3) Over the cleft in the bone the tissue is no more than mucous membrane, so very thin and delicate that failure to recognize this fact may be followed by failure of union. (4) The surgeon has so many operations from which to choose that he may be confused—(a) the soft palate may be denuded as it lies, by removing a strip of mucous membrane and the bared muscles sutured; (b) follow the plan elaborated in the next case (Fig. 8); (c) follow the push-back operation of Dorrance in two sittings; (d) follow the plan of Barrett Brown, in one sitting. This girl was 5 years old, well within the age limit for the push back operation and the degree of the cleft meant that the greatest distance in backward displacement could be obtained. This operation was performed by elevating the hard palate flaps, rupturing the posterior palatine arteries and replacing the flap in its original bed. Following this, she developed a middle ear condition, which is no objection to the operation, as it may occur after an operation of any kind. She did not re-

turn for 2 years. At the age of 7, at which time picture b was taken, I found that the mucoperiosteal flaps were twice the thickness of the original state, that the blood supply was so luxuriant as to be a matter of concern during the operation. It was controlled in this case by infiltration of adrenalin, 3 drops to 1 ounce of saline. The flap was so thick that ordinary sutures would not hold it to the bone, so I perforated the palatine process with wire, anchored it over a Brophy lead plate and held it with perforated shot. Then the soft palate was done, i.e., I did two operations at one time. On the sixth day, picture c was taken to show all stitches holding. Two of the deep stitches were removed, but such was her resistance that the removal of the last stitch was postponed until the next day, at which time, with all the operations and treatment, the little girl was in a frenzy. But I persisted in the removal and simply tore the wound apart, as shown in d. Here is an illustration of a failure which was due to a mechanical separation of the wound, without loss of tissue and it is offered as a caution for care in the removal of stitches. In spite of the fact that the hole in the soft palate will be nearly closed by contraction, it will be necessary to break the palate down, find the muscle, and perform a formal repair, as depicted in Figure 6a and Figure 6b.

cle with the superior constrictor of the pharynx at the hamular process but most operations on the soft palate, as I interpret them, fail to recognize the fundamental principle in wound suture, i.e., series layer sutures. The soft palate is repaired in the same way that I used to see laparotomy wounds sutured, with the Peasley needle. Through-and-through stitches will contract any denuded surface. Robert Ivy, of Philadelphia, has recently quoted Axhausen in a procedure in which the pharyngeal mucous membrane of the soft palate is sutured, the muscle bodies united by buried catgut stitches and then the oral mucous membrane approximated separately, which is exactly right. I fear the buried muscle stitch and believe some tension stitch should be used, because as soon as the muscle bodies are united, contraction takes place and pull against the

muscle stitches occurs. I favor removable stitches used in the form of a vertical mattress or of a figure of 8, i.e., the small and large bite stitches supplemented by single stitches in the mucous membrane, beginning on the oral side and carried around on the uvula to the nasal mucous membrane side, ending up at the posterior pillars. Precision is essential or one may get a postoperative result similar to the congenital condition shown in Figure 6a or a complete failure as in Figure 7b. To fill the dead space between the bone and the palate flap, Professor Veau has suggested the use of the mucous membrane of the vomer, which is used in the form of a flap dovetailed under the mucoperiosteum of the hard palate, thus filling the dead space. This flap so used closes up the nasal canal, but it does not close the cleft palate, to complete which it is necessary to suture

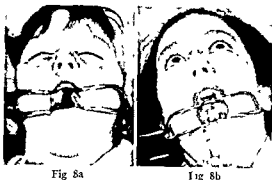


Fig 8a

Fig 8b

Fig 8 Group II Postalveolar process cleft, 2/3 The cleft in the horizontal plate and the palatine process is most evident. This is the easiest palate to do and with a minimum amount of traumatism. There is little to be gained by a push back. The mucoperiosteal flaps may be raised from the cleft margin. When this is done, the mucous membrane attachment of the soft palate to the horizontal plate of the palate bone is definitely demonstrated and easily severed, a necessary step and one I have used from the first palate operation I ever did. The ends of the tensor palati are positively identified and thus can be precisely sutured. The objection to denuding the soft palate by transfixation is that the tensor palati may or may not be evident. But contrary to the lip, in which no separate muscle bundles may be found, here there is an easily identified muscle, the suture and union of which are a crucial step in the repair. Should a failure of union take place there is still a cleft palate, and complete function cannot be expected. Lateral incisions may or may not be required, but they are usually used, because by so doing it seems to me that I accomplish to some degree at least the purposes of the more extensive push back. By far the most cases, by this simple procedure, obtain the aspect of a normal palate. This patient is now a beautiful girl of 16, who fully enters the social group of her age, has developed a fine singing voice, and who takes part in school operettas and platform speaking, so I believe that the steps of operation as outlined are primary procedures, and should a result be less satisfactory than in this case, recourse may be had with gratitude to the more extensive operation of the push back and its modifications. This girl has been recently checked up on speech according to the plan developed by Dr Wallace Ritchie. This test was done in the presence of a group of the family and office members, with instruction for each one to indicate even the slightest divergence from the normal. There were no comments, with the conclusion that her speech was absolutely normal. To me she is the support of everything I have said about the reconstruction of the palate. b. The spot in the picture on the soft palate is not a hole, but mucous membrane humped up into a red spot. The uvula looks like the one in Figure 9a, but of course is only a technical defect, in that the halves are staggered or the stitches pulled out. This condition has absolutely no effect on her speech.

Fig 9 a and b Group II, 3/3 The cleft extends to the anterior palatine foramen. It still has the aspect of a median cleft. This case brings up several problems of age for operation and proper operative procedure. I saw this child soon after birth. She was a very delicate child, with a cleft so wide that it seemed impossible to close. She was placed in the hands of a pediatrician who gave her the most careful attention, but it was not until the child was nearly 3 years old that I obtained his permission to operate, and then only because of my promise that the hard palate oper-

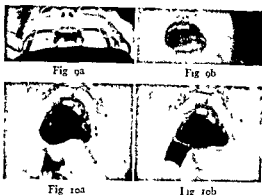


Fig 9a

Fig 9b

Fig 10a

Fig 10b

ation would cause no shock. The hard palate was infiltrated with salt solution containing 3 drops of adrenalin, which does control bleeding temporarily. The mucoperiosteal flap was raised from the cleft margin and the space behind it, and the bone was packed with a section of dental roll. This may be an excess of precaution, but so often I see that loss of blood in any operation seems to be in direct ratio to postoperative concern. The mucous membrane attachment of the soft palate was severed. Lateral incisions were made and packed with benzoid dental cotton roll, in an effort to release tension on the hard palate stitches, but also to hold the soft palate in the backward position. Lateral mattress stitches were placed in the hard palate in order to bring the periosteum into contact. The interrupted stitches were placed in the mucous membrane. By so doing, the fact that the covering of the palatine processes is composed of two different kinds of tissue is recognized. Mere contact of the edges of the cleft by a continuous or interrupted transfixation stitch invites defeat. In 6 months the posterior part of the healed hard palate was elevated and the mucous membrane of the bodies of the soft palate split, and the muscles sutured. To carry such a delicate child through a repair of the extreme cleft without a lot of concern from the postoperative condition and with complete primary union all along the line is what I consider a great victory, and this extended description is purposely made to support the sequence of operation. This girl is now 7 years old, very diffident, and retarded in general growth, and it is difficult to test her speech. What came through however, has a proper sound and her mother says she is readily understandable, which is not solid evidence to us, but she has at least a chance to improve, because the soft palate is movable. There was no chance to do a push back because a hole in the hard palate would be left and thus transfer a deficit behind to one in front. Should a gross speech defect become evident, the tissues are in position to follow the advice of Barrett Brown wherein the mucoperiosteum is split from before backward, leaving a covering of the cleft in the bone and the oral half pushed backward to increase the length of the soft palate. I have not done this but the enormous productivity of the mucoperiosteum is such that should occasion arise I would have no hesitation to follow Brown's technique.

Fig 10 Group II, 3/3 This is the same case as in Figure 9 but in the adult, with the same aspect of a median cleft. The older patients, even with an extreme degree of the cleft palate, depending somewhat upon the intelligence quotient of the case, speak intelligibly, having, by means of the superior constrictor of the throat, tried to improve the speech. Such a case can be done under local anesthesia but this case was done under general. The same operation



Fig. 11a.



Fig. 11b.

as discussed in Figure 9 was done, but here the hamular processes were fractured, a step used only occasionally and carefully done, because the styloid process in the point of contact of the tensor palati and the superior constrictor and a gross disturbance of the muscle position causes another break in the great muscle scheme of the throat. This cleft at the junction of the hard and soft palate measured 2 centimeters, which is the widest degree I have ever found and one feels justified in using every measure to reduce stitch tension. The follow-up picture is not so good, but both hard and soft palates united primarily. The same problems on future care arise as are present in Figure 9. In this a very intelligible speech, even with the wide cleft, showed a notable improvement, but an outstanding result lies in the improvement in morale of the patient which stimulates her to improve her speech.

If surgery is ever justified on psychological grounds, it is in these cases of young women and men who come of their own volition or through some agency. Characteristic is an inferiority complex, and an attitude of profound unhappiness in being different from their fellows often makes an appealing picture. Even though the operative result may not be complete, the mere fact that something has been done and that someone has been interested in them has in so many cases changed the whole outlook on life.

Fig. 11. Separation of the line of suture in the palate may occur at any time, in any case and in any operation. Failure with loss of tissue is serious, through not so much in the hard palate. Years ago in a group II, 2/3, case the right mucoperiosteal flap sloughed out, but such is the wonderful recuperative power of this tissue that the loss was filled in, so that now, at 10 years of age, the outlines of the loss are obliterated. Loss of tissue in the soft palate is a tragedy, because this means loss of muscle elements which do not reform. This case is one of my cases in which the soft palate failed, with gross loss of tissue. I shall be eternally grateful to Dr. George Dorrance in having the initiative and courage to work out his push back and demonstrate that these tissues may be freely mobilized to accomplish closure: a, is the picture after the elevation and replacement of the mucoperiosteal flaps, b, is the result of the re-elevation of the flap, and its suture to the palate bone. The soft palate tissues were so loose that it was possible to dissect and remove scar tissue, to find and suture active tissue together, with a result which, with any other method, involves the risk of a second failure.

Fig. 12. A 16 year old girl who gave no history of previous operation, but the condition appears so alike that in

the right and left mucoperiosteal flaps, which must be sewn so that the periosteum is definitely in contact. I do this by using a lateral



Fig. 12a.



Fig. 12b.



Fig. 13.

Figure 11 that I feel that someone else obtained a failure of primary operation. I thought I would use the technique which was so complete and satisfactory in a cleft of similar degree to that used in case shown in Figure 8 b. In this case it was necessary to make an incision at the heel of the process for the insertion of New's elevator, the soft palate was then severed from the bone, the hamular process fractured, the lateral incisions extended to whatever degree is thought necessary. The incision was packed with dental cotton roll soaked in tincture of benzoin, cut to fill the incision snugly. The hard palate mucoperiosteum was sutured and the operation concluded, to be continued at another sitting, at which time it was found that the soft palate could be easily handled, the muscles found on each side and sutured together. The result was a primary union as shown in b. These older cases are most satisfactory because the patient knows what is being done for him and is most co-operative. Certainly the result in this case looks better than that in Figure 11, and was obtained by much simpler procedures which are applicable to secondary repairs as well as primary. In fact, I think I have unwittingly been doing a push back to some degree for many years.

Fig. 13. In about 4 in a hundred cases, a combination appears in which the lip is cleft, the process is normal and the palate is cleft, usually in the 1/3 or 2/3 degree. The lip is recorded as group I and the palate as group II. The clefts are repaired by the steps outlined previously in these two groups.

mattress stitch supplemented by single stitches in the folded ridge of mucous membrane. Mere contact invites defeat. Dr. Dorrance

has suggested that the mucoperiosteal flaps be skin grafted, a procedure which I have not carried out, because the field seemed too unfavorable for a "take." But the Veau operation works, and, although it is most applicable to the group III palate, I have had the courage to do it in two year old group II, 3/3, cases, without a bit of reaction and with perfect union of the palate. In fact, the operation on the hard palate produces no reaction. It is only when the two operations are done at one time that any concern is felt over the condition of the child or the outcome. The greatest satisfaction I have had is the recognition that two operations are involved, the hard palate and the soft palate, but my greatest difficulty is in deciding to close them at different sittings, and to do the hard palate first despite criticism of men of wide experience. Some of my colleagues shudder when I reveal what I am doing.

I think the Warren Langenbeck operation is a fundamental one and it is up to us to supplement it by modification of technique, age for, or sequence of, operation. The lateral sliding flaps on the hard palate, supplemented by the vomer flaps of Professor Veau, open up a vista of progress, which may end in a goal of success and answer the objections and erase the many personal opinions as to how it should be done and thus put a quietus on the effort to present some slight technical modifications, many of which are simply confusing to me. I have included in the pictures some secondary repairs because I have found that no matter what the meticulous effort, there are so many uncontrollable factors in the repair of cleft palate inimical to primary union that failure may occur at any point or all along the suture line.

#### GROUP III. THE ALVEOLAR PROCESS CLEFT THE GROUP III CASES

I once tried to find some percentages of incidence of the various combinations of the clefts, and while there were so many factors of error that no exact figures could be made, the indications were that most of the cases come with cleft alveolar processes. There are three subdivisions in this group, the unilateral, the bilateral, and case with a normal hard and soft palate. Broadly stated around 60 to 70 per cent of all cases appear in this group. The



Fig 14a

Fig 14b

Fig 14. Group III, left complete. In this case all the clefts are present on the left side, and thus the normally developed tissues are apart from the vermilion border of the lip to the uvula. a, Shows the most frequent case. The process cleft measures 8 millimeters. The average runs from 6 millimeters to 12 millimeters, below 12 millimeters down to a notch, above 12 millimeters up to 18 millimeters, which is the widest cleft on my records. This is the case on which I used to put the wires in the maxilla, with what seemed to me satisfactory immediate results. On account of observation of the babies' growth, I discontinued their use, because I saw so many cases grow up with narrow jaws, and malocclusion of the alveolar process with the mandible. This did not always happen, but enough cases of gross surgical deformity occurred to lead me to discontinue such methods in favor of manipulation and the construction of a movable active lip, which, by its action, exercises an enormous influence, not only on the process, but on the whole bony structure of the upper jaw. If by thumb pressure on the premaxilla, which is seen peeping out from behind the prolabium, the premaxilla can be brought down to the maxilla out of contact to 4 millimeters or less and the lip down over it, it is a constant observation to show the process closed by the time the stitches are removed from the lip. This happened in this case, because the premaxilla had healed on to the right maxilla quite symmetrically in the curve of the whole process. b, The postoperative picture as the baby left the hospital, with the vermilion border well aligned, eversion of the mucous membrane and the floor of the nostril made with some irregularity of the left lower cartilage of the nose. This baby is a complete case, with primary union in the hard and soft palate, done in exactly the same way, as outlined in the group II cases. The process is closed and the lip has hardly a perceptible scar.

process cleft cases show the greatest variation in development and position of the frontonasal process. The maxillary processes, right and left, appear to be normally developed. In the bilateral clefts the degree of projectional displacement of the premaxilla and prolabium give a great variance to the picture of the case. In the unilateral case, the pivotal and rotational displacement of the premaxilla, healed normally to one or the other maxillary process, gives the degree of the cleft, which in turn gives the great variation in the picture of the

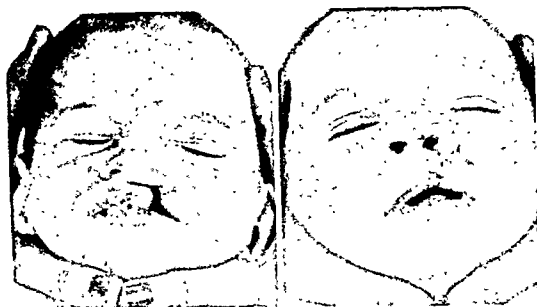


Fig. 15a.

Fig. 15b.

Fig. 15. Group III, unilateral, left. This shows a case similar to that in Figure 14, but here the premaxilla has healed on to the right maxilla, with a definite degree of projection and rotation. I saw this baby at birth and put on adhesive straps extending outward on the cheeks and incorporated in the straps a rubber band, intending to get continuous traction in the curve of the normal process. The plan had some effect in narrowing the cleft to a point illustrated, a, but it was not complete. It was the same result that I obtained when I was using wire. Nothing really happened until the lip was done. At 6 months this case was manipulated and the lip done over a 4 millimeter cleft, with closure of the bone cleft. b, The lip looks about as usual, but the nostril is too wide open and the alar end of the cartilage too low. This boy is growing up with a flaring nostril, not of severe degree, but not perfect. This is also a completed case, with primary union in both hard and soft palate. The only question involved is the development of the nose.

Fig. 16. Group III, unilateral, right complete. This case is the reverse of that shown in Figure 15, with the same disposition of the tissues, except that the premaxilla has healed to the left maxillary process, in a position of at least 45 degrees' rotation. The outlines of the prolabium are not so definite. By reason of the rotation the columella is also decentralized. The nasal cartilage is extremely flattened. There is here also a choice of the preliminary use of wires and plates to close the process cleft forcibly, or the manipulation of the premaxilla and the reconstruction of the lip and nose, or the use of the vomer flap on the hard palate to be followed by the lip repair. The latter plan seems now to be popular and I have done it with varying ease and satisfaction, usually depending upon the degree of the process cleft. Such a procedure means two operations at one time. Since I believe that the use of the vomer flap is an accessory step in the closure of a hard palate cleft and can in no way substitute the median suture of the mucoperiosteal flap, and since I believe that a movable, functioning lip is essential to future growth, my tendency is to take the spring out of the bones, reduce the process cleft as far as possible and build the lip over it to complete the closure. b, This was done in this case. The operation of mobilization of the tissue, the muscle suture of the body of the lip, the construction of the nostril, and the centralization of the columella all require time and any extension of the operation seems to me to invite trouble. For these reasons I have often put off the vomer flap until the hard palate operation. Both the vomer flap and the suture of the mucoperiosteal flaps can be carried out at the same sitting without causing any shock.



Fig. 16a.



Fig. 16b.



Fig. 17a.



Fig. 17b.

Fig. 17. Group III, unilateral, right complete. Another case similar to that in Figure 15. The degree of the process cleft is entirely due to the pivotal displacement of the frontonasal process and of course, the left maxilla in this baby is displaced outward secondary to the position of the vomer and premaxilla. To move the premaxilla and the whole maxilla requires positive force, and in a 14 millimeter cleft it is never complete and has a tendency to spring back. I have faithfully used outside force, by adhesive straps and rubber bands, and a suggestion made by Dr. H. R. Allen of Indianapolis in which a clock spring instead of the rubber bands is incorporated in the adhesive strap. I have been able to gain as much as 6 millimeters, but there never was complete closure by such methods. So tragic were the late results in those cases where I used direct force through wire, that I have promised myself never again to insert them in the upper jaw, but I have wondered what penalty would be paid in putting in some material to hold the premaxilla down until the lip was done. Of course, such a wire or silk worm would encircle the premaxilla and thus possibly inhibit circulation to the front incisors and interfere with their normal development. When I first suggested the circular wires applied in the curve of the process, Dr. W. H. Logan of Chicago made this criticism and I am able clinically to support his contention. I believe it better to take a chance of manipulation of the premaxilla and lip repair. If the process cleft is not closed, it is possible later in life to insert a lateral incisor, which so often comes in deformed anyway. b, Compare this nostril with that shown in Figure 17 a. The cartilage is nicked, the floor of the nostril was better than the picture because it was not cleaned off. Can anyone explain why in one case the outcome is acceptable and in the other deformed?



Fig 18a



Fig 18b



Fig 19a



Fig 19b

Fig 18. Group III, left complete. Secondary repair. The muscle theory repair of the lip fits perfectly into the secondary repair of the lip. a, Shows an incomplete repair with a flaring nostril, no floor to the nostril, a notch at the vermillion border, and what looks like the result of the old harelip operation. To prevent such results many operations have been devised. The lip must be broken down and the scar tissue removed to find the ends of the active tissue and the technical steps followed as outlined in Figure 1.

Fig 19. Group III, right complete. This case is included because the girl shows unacceptable results in both the lip and hard palate. Her chart shows originally a 10 millimeter cleft process and a 14 millimeter measurement at the junction of the hard and soft palate. The process was manipulated and the lip done. She was quite sick, the upper stitches of the lip became inflamed and the wound separated. The lower stitches of the lip pulled, with the resulting deformity of the nose and floor of the nostril and the red border included in the lip wound, a condition similar to that in Figure 18a. So concerned were the family that she did not return until 5 years of age. The process cleft was closed and the front incisors appear normally placed. The measurement at the hard and soft palate was now 10 millimeters, i. e., in the interval, by waiting, the tis-

sues of the hard and soft palate were brought 4 millimeters nearer to each other, either by growth or indirect pressure of the coordinated expression muscle groups, or simply by weight of the soft tissues of the upper jaw, or all these factors together. I have seen this occur quite constantly, and if others support the observation it may be an argument in support of Dr Dorrance's opinion that the cleft palate should not be repaired until the age of 4, 5, or 6 years, at which age it would be expected that the maxillae are fixed and set to resist any possible effect of scar formation or contraction on their normal growth and thus meet the objection of the dental surgeons. At this age also it may be reasonable to do both hard and soft palate operations at one sitting, as was done in this case. The Veau flap would be difficult to cut, if not impossible in this case. In 19b, the hard and soft palate closed primarily. The hard palate shows the projecting ridge built up by the lateral mattress stitch used to bring the periosteum in contact. This usually disappears as in Figures 6, 7, and 8, but once in a while it stays with no disability except that of a cosmetic deformity. The soft palate is long, flexible, and has perfect function for speech. This was a public case and such was the attitude of the family that it is difficult to get them to consent to further surgery, but I predict she will come of her own volition later to have lip and nostril corrected.

palate, while in the lip the width of the cleft is entirely secondary to that of the process cleft. The picture of a median cleft palate is lost, although in the bilateral case it is often evident.

While the lip and palate problems are present, they are in more extreme degree than in group I and group II, but added to them is a bone cleft around the proper care of which has raged the greatest diversity of opinion. In fact, the group III, unilateral, being the most frequent combination of the clefts, has been the subject of most of the literature. This case has been called the single complete hare lip and cleft palate, which fairly describes most of the cases. This description puts the alveolar process into the palate, and the treatment of this cleft has been included in the procedures called cleft palate operations. The embryology indicates, however, that the alve-

olar process is formed in relation to the lip, and therefore the care based on the idea of a whole or complete cleft palate is an incorrect premise.

Because of the fact that the process cleft was evidently in the bone, the idea was carried to the whole palate, and since bone is the most resistant of all tissue, some kind of force is necessary to move it. Hence there appear in the literature many plans, all collected by Dorrance in a chapter called "Uranoplasty by Compression Methods." The late Dr Brophy was the outstanding sponsor of the use of compression methods and his ingenious plans are given in a special chapter in the "Operative Story of Cleft Palate." So influenced was I by his theories, arguments, and practical experience that I undertook to follow his suggestions and I have not yet recovered from my surprise that the cleft palate was not closed, and



Fig. 20a.



Fig. 20b.



Fig. 20c.

Fig. 20. Group III, with a normal palate. In about 10 to 20 per cent of the cases there is a case of cleft lip, a cleft process, and a normal hard and soft palate. These cases are the clinical support of the embryological fact that the alveolar process is not a part of the palate, but has a definite origin of its own, and is formed in relation to the lip. In most of these cases, the alveolar process cleft is not wide and the case often presents the problems of group I, pre-alveolar cleft, but on about 4 occasions I have had a case in which an apparent overgrowth of the premaxilla presented an added problem in repair. I present this case because it brings up a problem once discussed in the literature—the removal of the premaxilla. In a, it is to be observed that the processes of the right and left maxillae are near together with only a small triangular space between them, in perfect shape and position to receive the premaxilla, had it not been so large and so projectionally displaced. This triangular space is only evident in this combination of the clefts. In the embryology apparently the fore part of the palate is filled in, not by mucoperiosteum, but by tissues developed in the frontonasal process, which is another argument for the Veau vomer flap. Clinically I have found that the vomer flap is most satisfactory for the forward third of the palate, but if the flap is used as a lining for the mucoperiosteal flaps, it should be carried back as far as possible, which I think is all right, provided the mucoperiosteum is sutured at the same time. Unless this is done in the hard palate and the operation continued to include the soft palate at the same time, it is impossible at a later date to sever the soft palate from the horizontal plate of the palate bone without disturbing the vomer flap, and in some cases I have had to undo the first operation. In b, the extreme projection requires a repositioning of the premaxilla, but in this case the size of it was too large to fit into the triangular place, even



Fig. 20d.

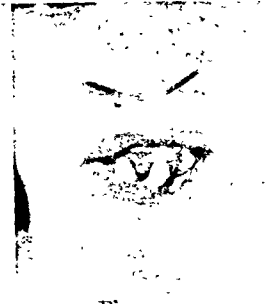


Fig. 20e.

if it could be pushed back, so I decided to do the lip and see if the rest of the face would grow up to the premaxilla. In c, the result of the lip repair. Both sides were done at one sitting. d and e, I let her go until school age, but her deformity was so terrible that I decided to remove the premaxilla and have a premaxilla built on a denture later. This is the only time I have removed a premaxilla, although at one time this procedure was advocated by distinguished surgeons. Of course, it should not be removed, except for some such reason as has been stated. e, Shows the process cleft still present. I have similar conditions in the unilateral case in which the indirect force of the lip has not closed the bone cleft, either due to the width of the cleft or the rigidity of the bones in the case, and a similar deformity is left. It is such observations that have led me to advise that all cases of alveolar process cleft be attacked at an arbitrary period of 6 weeks—at least before 3 months of age, while the bones of the jaw are still soft and pliable, not on account of the lip or palate cleft, but on account of the process cleft.

that the main achievement was the closure of the alveolar process cleft. The hard palate and soft palate subsequently had to be repaired and, although the cleft appeared narrowed, it was necessary to mobilize the hard palate and denude the soft palate. I have found the report of no case in which the palate has been closed by compression methods. The methods incurred in my hands a penalty of overcorrection that seemed to be a worse deformity than the original condition, but I still felt that some form of direct force was necessary to close the cleft in the process and proceeded to suggest a plan which purported to influence this cleft.

The results were so poor that I revised the whole chapter in order to pull out this part on compression methods. Dr. Dorrance complimented me by including the plans in his book, and, although I think the arguments for it are logical and theoretically correct, practically the results were terrible and I shudder to think of the babies whom I have subjected to such methods. However, the hard palate and soft palate techniques have held up with such constant satisfaction that I resubmit them. But should anyone be interested enough to review that part about the wires applied to the upper jaw, please consider it blacked out.





Fig 21a

Fig 21b



Fig 21c

Fig 21d

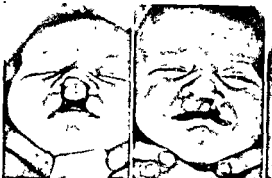


Fig 22a

Fig 22b



Fig 22c

Fig 22d

Fig 21 Group III, bilateral. a, In most of the cases the premaxilla is centrally placed and here is the picture of the most frequent case. I early found out that there is no muscle tissue in the prolabium, and yet in the normal lip there is muscle. At first I did both sides at one operation, and I found that I could obtain a satisfactory skin closure with out crossing stitches, but the results all looked to me like curtain lips. So I decided to do one side at a time and try to bring the muscle bundles to the midline of the prolabium and, at a later date, do the same thing on the other side, that is, do two unilateral lip operations at different sittings. The attempt is made to incorporate the prolabium in the lip. This is in direct opposition to the opinion of many surgeons of wide experience who believe that the prolabium is a part of the columella. b, The result of the first operation on the left side, in which the slight rotation of the premaxilla is overcome by the force of muscle pull. c, The picture of the lip as the baby returns for the other side, after a 6 weeks' or 2 months' interval. d, The lip completed, with the right and left expression groups, if not in contact, at least anchored in the direction of the normal action. This case was completed by doing the hard palate in the next step and then the soft palate, as outlined in the group II cases.

Fig 22 This is another average case, with a bit more projectional displacement of the premaxilla. The prolabium is well developed, but does not move on electrical stimulation. It is about the limit where it may be expected that the lip will completely bring the premaxilla down to the maxilla on either side. One may try to learn by thumb pressure how near the process clefts may be closed. The trouble is that the premaxilla may spring back, or if the distance is too great, a bend in the vomer and septum occurs which may be of such degree as to obstruct the nasal chan-

nel. If this occurs the vomer must be sectioned. There are several ways, and I have tried them all, and have discarded any procedure that entails removal of any part of the vomer. The square piece or triangular piece removed just back of the premaxilla has been discontinued because not infrequently this step resulted in a movable premaxilla, but the main reason was that it caused an inhibition of growth and atrophy of this essential structure of a normal process. I have cases growing up in which the premaxilla has failed to develop to a point that looks as though I had removed the premaxilla. I have tried removal of a square piece from the middle of the vomer, and although the premaxilla develops normally there still may be free motion of it. So I have selected to fracture the vomer about the middle, by reflecting the mucous membrane back, exposing the vomer. The fracture is made with a chisel and in an oblique manner as possible. This permits sliding the forward half backward on the posterior half. The direction of the cut shall be pointed forward to the cleft opposite to the lip cleft which is to be repaired. In this case it was directed to the left cleft, and the right cleft lip repaired. b, The pull of the right facial group on the prolabium and the columella is well shown. This pull is also on the whole forward half of the vomer, to hold the raw surfaces together, and it is the greatest satisfaction to find that in Figure 22c bony union of the fracture has taken place. The premaxilla is replaced in contact with the maxilla surely on the right side and almost on the left. The picture shows the muscle bundles of the right side tucked in under the prolabium. It is not possible to do this so well in all cases, but that is the purpose. c, Shows the result of the second operation on the left side, which also completed the closure of the process cleft. d, Shows the boy as he returns for the hard palate to be followed by the soft palate at a later date. The pro-



Fig. 23a.



Fig. 23b.



Fig. 23c.

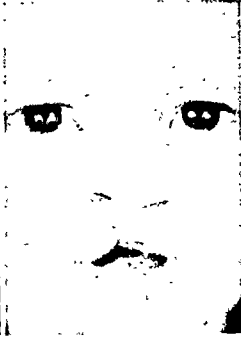


Fig. 23d.



Fig. 23e.

labium has had a chance to grow. One may criticize the width of the nostrils and the depression of the tip of the nose, but there is a look of comfort which I believe is due to the fact that his expression group of muscles have been co-ordinated.

Fig. 23. a, This case shows the extreme pivotal displacement of the frontonasal process to the right. The baby just missed being a left unilateral case. The not infrequent picture of the tongue lying in a process cleft has been used in support of the proposition that in the etiology of these clefts, interposition of the tissues is a factor. In the lip the tissues of the right maxilla are partially in contact with the probabium, with probably some muscle fibers migrated over, so it is quite constant to obtain some motion in the probabium by electrical stimulation. b, The premaxilla is in contact with the process of the right maxilla, doing so by rotating to the right. The projection is not great and a removal of a piece of the vomer may pay a penalty of replacing the premaxilla too far back. It has now become the form to do the Veau vomer flap on one side and the cleft lip on the same side at the same sitting, thus presenting another reason for doing a bilateral lip, one side at a time. This reason is different from the one upon which I have been working, which is that I have found it the easiest and most direct way to line up the muscle bundles underneath the probabium and thus co-ordinate the right and left facial groups of muscle. In other words that the bilateral lip is simply two unilateral clefts in one case. In this case, I elected to reflect the mucous membrane of the vomer and

obliquely fracture it about the middle with a chisel. The forepart of the fracture pointed to the incomplete cleft of the process and lip and I proceeded to do the left lip cleft. c, The picture of the baby when it returned for the right incomplete cleft, with the premaxilla centered and the vomer rigid. The right nostril is too wide, and although the lower nasal cartilage is improved, it is not perfect. It is most difficult to line the vermillion border exactly. Apparently the line is perfect on the left side and incomplete on the right, but the lip appears normally prominent. d, The picture of the lip and nose as the baby goes home after the first palate operation. The immature probabium in Figure 23a has grown downward. The vermillion border of the probabium is a part of the red border of the lip. Any divergence from the normal is purely a technical result. e, The palate shows the result of suture of the mucoperiosteal flap and the complicated palate has been changed over to the group II, 1/3. Everything is done except the suture of the soft palate muscles. This was done later, with primary union.

In this case the use of the Veau flaps before the premaxilla was centered or done in conjunction with the lip would have carried a risk of failure. But of course it is easy to line the suture of the lateral sliding flaps. I have found that the vomer mucous membrane heals kindly after the vomer fracture, but of course both operations, the fracture and the Veau flap cannot be done at one time, so in these extreme cases the problem of sequence of operation is most important.

### GROUP III. BILATERAL

In these cases the right and left maxillary and the frontonasal embryonal processes are out of contact all along the line. The consideration of the subject should really begin with the study of them because all combinations and degrees of clefts in the group I, group II or the unilateral subdivisions of group III are simply exhibitions of failure of contact of these three embryonal processes at this or that point, or complete union of the normal, or complete disunion as here shown. With this picture in mind, it is possible to determine in any case what has or has not happened in that case, and with the picture of the normal baby in mind, one is in a position to decide what

should be done surgically to correct the defect. Of all of the parts involved, the greatest variations in development and position are not in the lip or the palate, but in the vomer and premaxilla. The vomer at times is sturdy, again thin and wafer-like. In the unilateral case the vomer mucous membrane may be widespread, a definite structure easy to handle, or thin and delicate, difficult to handle without perforation. The premaxilla shows wide margins of projection, as in Figure 17b, or extreme rotation on its stalk. The probabium of the lip may be small and undeveloped to a point where it seems hardly worth while to use it, or it may be a definite structure with sufficient body to hold stitches.



Fig. 24 Two cases of bilateral lip repair are compared. In a, left, operation was directed to repair of the lip and the reconstruction of the nose was secondary. In b the purpose was reversed. These 2 cases are presented in support of an observation that the repair of a complete cleft of the lip, both unilateral and bilateral, entails the consideration of two operations divorced in principle, viz., in a, an anatomical replacement of active tissues out of contact in the

#### SUMMARY AND CONCLUSIONS

The series of cases here presented gives one only a glimpse of the many combinations and degrees of the cleft which present themselves for correction. These cases were not selected to show good or bad operative results, but each case shows average degrees and combinations and in the main are presented to indicate the applicability of the classification to describe the case. Comparison of the group I and group II cases with the group III cases clearly supports a proposition made in 1920, viz., the alveolar process is a basis for the surgical grouping of these cases. I believe that the most important requirement of progress in this field is some kind of nomenclature and descriptive terms to substitute the loose and indeterminate terminology of harelip and cleft palate which permits the same case to be described in several ways according to the opinion of the observer. The special term "harelip" is misleading and has fostered the presentation of operations, which, on analysis, are simply plastic procedures which represent the personal opinions of the sponsor, as to how the operation should be done. "Cleft palate," is also misleading, as its use is made to describe a whole palate and thus fails to indicate the presence of several kinds of tissue. No direct mention is made of the alveolar process, the condition of which is so important to the

lip, with function a prime purpose, and in b, a plastic repair of inactive tissues of the nose, with cosmetic result a prime purpose. These are surgical principles recognized elsewhere in the body, but ignored in this field. In b, the surgical principle of the nose repair is carried to the lip, the mucous membrane of the prolabium is sacrificed, and the maxillary tissue sutured below the prolabium. b, is only one of the results of trying to place the prolabium of the lip into the nose.

I can show cases in which the prolabium, left in the lip, having no place to grow, has bunched up like a mattress. I can show cases in which the maxillary tissues below the prolabium have grown so that the lip became inordinately long, but most of the b cases are curtain lips. Figure 24b shows the boy, showing the limit of his motion. He has a flap upper lip due to the fact that the muscle bundles have not developed, because it is repeatedly demonstrated that muscle tissue atrophies on disuse. In Figure 24a, I felt that I had a definite purpose in replacing the tissues according to the embryology, the position of the parts supported by clinical results in the group I cases and the group III unilateral cases, while in b I was simply doing something on my own hook. In a, an unsatisfactory result would be a technical fault. In b, an unsatisfactory result would be due to a failure to recognize surgical principles. Every evidence points to inclusion of the prolabium into the lip.

case. With failure to recognize the character of the structures involved, we have the Langenbeck, the Lane, the Brophy, the Veau, the plan sponsored by Dr. W. B. Davis, and the Dorrance push back operations and their modifications for cleft palate. The presence of a cleft alveolar process produces a startling picture, but I see no reason to believe that the conclusions of the group I lip and their forms and degrees are directly due to the disposition of the muscle elements or the conclusion of the group II case, that the clefts of the hard and soft palate are median clefts or that the character and texture of the tissues are changed because of the presence of a factor entirely outside their structure. Because of the dual point of view of harelip and cleft palate, I find contributors interested in one or the other. I believe we should be interested in the case as a whole, to study it as an individual and to select a procedure which will not exceed the possibilities of the tissues in mobilizing and suture. I early decided that the way to close the clefts was already in the literature, and, although other operative steps have been suggested in the past few years, these newer ones, the Dorrance push back and the Veau vomer flap, while gratefully accepted, appear to me not fundamental changes, but accessory steps which it is possible to do, not as a rule, but in selected cases, the push back applicable to the

group II, 1/3, case, the vomer flap to the group III unilateral, where it may be used for three reasons: to close off the nasal canal, to fill in the triangular space back of the premaxilla, and to line the mucoperiosteal flap. It is acceptable on all counts, but the fundamental requirement in the repair of a cleft hard palate is the suture of the mucoperiosteum. In many technical operations a fundamental principle in wound repair, layer or series sutures, is ignored. The fact that transfixation sutures narrow the contact of denuded surfaces is not considered. This is seen in the soft palate, as in the Brophy operation or in the old harelip pin operation for the lip, wherein the contact of the body of the lip was narrowed and only mucous membrane and skin were united. Also in the hard palate, the flaps of which are composed of two of the most vital tissues in the body, mucous membrane and periosteum. Warren probably sewed the periosteum but did not mention it, and it remained for Langenbeck to indicate its importance. In spite of this, I have seen the flaps sutured in the midline with a continuous running stitch, or with delicate needle and suture material, which may or may not include both tissues. It is wise to be sure, because the end-on or vertical mattress, or better, the lateral mattress for one series sutures plus single stitches for the raised up mucous membrane are exact. Sometimes it is overdone, but usually it smooths out, as in the group II palate.

I can remember only one case in which the lateral incisions did not promptly heal in. Of course, the dental surgeons and their reports on the growth of the upper jaw are most disturbing about median closure of the hard palate, and two proposals must be considered: first, the use of the vomer flap to line the mucoperiosteal flaps, or a postponement of the hard palate operation until patient is 4 or 5 years old, as so definitely advised by Dorrance. At that age the maxillae would probably be so set that any contracture would not influence the future growth.

And so I conclude the presentation, feeling that many phases of the subject have not been covered and that much repetition has been made. It was difficult to curb the desire greatly to augment the number of cases shown

because, in reviewing the records, each case has some special story of experience and results. After 25 years of interest in this subject and the care of over a thousand of these cases, I believe that the future progress depends upon the discussion of and agreement on surgical principles. Based on the findings in embryology, anatomy, and physiology as outlined in previous discussion (5), and the clinical presentation here made, I repeat some principles upon which to work in the future:

1. The approach to the subject shall be changed over from the dual point of view of harelip and cleft palate to the idea of a series of congenital clefts which involve the face and jaws.

2. The lip cleft shall be approached as a break in the great muscle scheme of the face, which involves the consideration of two separate operations: an anatomical replacement of the active tissues of the body of the lip plus a plastic repair on the inactive tissue of the nose.

3. The alveolar process is a definite entity of as much importance if not more so than the lip or the palate. It is not a part of the palate, so that the compression methods, such as the Brophy cleft palate operation, have been established on an incorrect premise and should be discontinued. The complete cleft palate of the literature is a combination of two clefts involving the handling of bone tissue in the process plus a plastic repair on the inactive tissues of the hard palate.

4. The soft palate cleft is a problem similar, if not identical, with the lip cleft—an anatomical replacement of active tissues out of contact, and the cleft of the soft palate is again simply a break in the great muscle scheme of the throat. Contrary to the lip cleft, it is possible to identify a muscle such as the tensor palati, the precise suture and union of which is a great essential to successful function of the soft palate.

I early concluded that the muscles of the soft palate did not work against the bone, but against the tensor palati, and it made no difference where the tissues of the soft palate were, so long as this muscle was united. In order fully to identify it I found it necessary to sever the mucous membrane attachment of the soft palate to the horizontal plate of the

palate bone. Thus, after accepting and performing the push back of Dorrance and comparing results, I think I have unwittingly been doing the push back for many years. However, the point of importance is that the operation I have been doing is applicable to the group III palate as well as the group II palate. My greatest unsolved problem is to construct a deformed nostril to look and grow like the normal one.

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<sup>1</sup>Davis advocates the inclusion of the palatine process in the lateral sliding flaps, which are usually sutured with interrupted wire sutures, thus erasing the possibility of scar formation which may interfere with development of the upper jaw, a late development when the mucoperiosteal flaps are raised from the bone as in the Langerbeck.

<sup>2</sup>The outstanding contribution to this subject in recent years in which Dorrance has collected and filed the operations presented from the beginning of accessible literature with historical comments and a complete bibliography. He presents an original operation for the group II palate.

<sup>3</sup>Ivy quotes Ashhausen and presents his diagrams. He also presents diagrams from Veau. He reports the use of a combination Ashhausen and Veau in the group III unilateral and bilateral cases and the Ashhausen in the group II cases, with specific statements of the age for operation. This is a very valuable paper, not only in the form of the presentation but in the reasonableness in conclusions and performance.

<sup>4</sup>Beautifully written and illustrated paper of operations he has selected and done, with logical reasons for their choice.

<sup>5</sup>An effort which purports to change the approach to our various problems from a viewpoint other than that of bare lip and cleft palate.

<sup>6</sup>Defines early closure as operation in the first month of life and late closure to be after 3 months. Shows several cases done at 12 hours and at 3 days, with excellent postoperative results.

<sup>7</sup>Advocates early lip repair, the first day or first week.

<sup>8</sup>A concise, yet complete and very orderly presentation of the subject, with diagrams and clear discussion of the many lip operations, as well as the process and palate procedures, which recognize that the alveolar process cleft is an entity separate from the hard and soft palate.

<sup>9</sup>This is but one of a series of monographs written by a master surgeon. Others deal with the lip repair, one on the embryology and on other phases, so that the series covers most of the field. With the war disrupting channels of communication, these pamphlets have increased value. I have them on file in the library of the Ramsey County Medical Society in St. Paul.

# THE TREATMENT OF COMMINUTED FRACTURES OF THE OS CALCIS

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THE problem of treating the *crush* fracture of the os calcis with displacement and comminution into the joint is well appreciated, as is evidenced by the numerous contributions to medical literature dealing with the reduction and end-results of this fracture. From the many methods of treatment advocated as well as from the variable results, it may be concluded that no method proves entirely satisfactory in all cases.

On the other hand, there is no doubt that definite progress has been made in the treatment of these fractures during the past decade, and studies of end-results show an appreciable decrease in both the temporary period of incapacity and the amount of permanent disability.

In connection with the treatment of these severely comminuted fractures, the question arises as to whether perfect function can be restored in all cases by any method. The subastragalar joint involved is a weight-bearing joint, and the integrity of its articular surface is vital to the mechanics of walking. It is difficult to secure accurate replacement of the individual fragments, and in the event of imperfect alinement, the joint no longer functions properly and arthritic changes subsequently develop. Even when an apparently exact restoration of the joint surface has been obtained, arthritic changes develop as the result of periarticular damage and from bearing weight on the roughened joint surfaces. Another factor to be considered is that these fractures occur almost exclusively in working men, many of whom before sustaining the fracture have a "wear-and-tear" arthritis. A perfect recovery cannot be expected in such cases any more than in severely comminuted fractures of the ankle or knee-joint that are complicated by arthritic changes (Figs. 1 and 2).

From the MacAusland Orthopedic Clinic.

At the present time the methods of treatment in use range from simple immobilization without reduction of the fracture, through dislodgment of the fragments by manipulation or by a crushing force and molding of the fragments into position, through traction measures, to operative reposition or early arthrodesis. Plaster fixation alone is no longer considered an efficient form of treatment, and the great majority of surgeons are of the opinion that an attempt should be made to reduce the fracture. A survey of a series of cases that were originally treated by plaster fixation, and years later were seen at our clinic, showed clearly the inadequacy of this treatment. There were 43 fractures in the series. All patients, with the exception of a few who had a solid ankylosis of the subastragalar joint, were permanently disabled. The deformity persisted, the os calcis being shortened and broadened and pulled upward. The patients complained of sore, painful, and tender feet and of restricted motion. Not one of the patients had been able to resume his former occupation, but several were doing a lighter form of work.

Reduction by manipulating the foot over a vertical bar and molding the fragments into position (Yoerg) may be difficult because of the great force required to free the fragments and pull the tuberosity downward. The dislodgment of the interlocked fragments by the blows of a hammer (Hermann and Pretty) would appear to subject the os calcis to a traumatic and uncontrollable force. However, both the manipulative and hammer methods have a certain following, and good end-results have been reported in fairly large series of cases.

Operative reduction has been advocated particularly by French surgeons (Lenormant and Wilmoth) as the most satisfactory treatment when the fragments that include the subastragalar articular surface are depressed

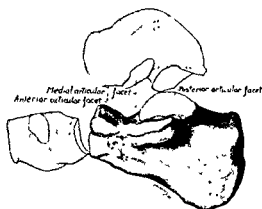


Fig. 1. The three articulating surfaces of the os calcis and astragalus. Viewed from the medial aspect.

into the body of the os calcis. Recently Murray advised this procedure in such fractures. The operative method consists of elevating the upper cortex of the bone to restore the articular facets to normal position, and securing fixation of the replaced fragments by means of a metallic osteosynthetic material or by osteoperiosteal grafts. The method obviously has a limited field of application; it necessitates operative trauma and hence more atrophy; and it is difficult to pry fragments bearing articular facets into normal position and insure their fixation.

Arthrodesis has a place in the treatment of comminuted fractures of the os calcis, not as a primary measure, but as the treatment of fractures of long standing with persistent pain, sensitiveness, and restricted motion, in which conservative procedures proved ineffective. The fact that many good functional results are obtained by reduction is an argument against the immediate sacrifice of the joint. There are, furthermore, certain contra-indications to performing an arthrodesis in fresh fractures; not only is it difficult to carry out the operative technique in the presence of disorganized articular surfaces and damaged tissues, but also there is the danger of infection.

Of all forms of treatment, traction methods are the most generally accepted. The outstanding traction method is that advocated by Boehler, and more comfortable, weight-



Fig. 2. The typical squash type fracture of the os calcis with disruption of the joint surface. Viewed from the lateral aspect.

bearing, and functional joints have been obtained by this method than by any other procedure (Stewart, Carothers, Jackle and Clark, Schofield, MacAusland). An alternative method of traction that is finding favor in Germany has been used by Ehalt and by Westheus. It consists of introducing a transfixion pin into the posterior fragment of the tuberosity and using it as a lever to force the tuberosity downward. Lateral deviation is overcome by means of a compression clamp.

The technique of the Boehler method is so well known that only a few features will be emphasized. In brief, the method consists of (1) freeing the interlocked fragments by manipulating the foot at the subastragalar and midtarsal joints, (2) restoring the normal so called tuberosity-joint angle by traction, (3) restoring the length of the os calcis by traction, (4) correcting the lateral broadening by means of a compression clamp, and (5) maintaining fixation and protection until union is firm. In the dislodgment of the fragments, as complete motion as possible should be obtained in the subastragalar and midtarsal joints. If necessary a Thomas wrench, or a wooden wedge over which the foot is buckled, may be used to secure free motion. Traction is established by means of two transfixion pins and the Boehler screw traction apparatus. Some objection has been raised against introducing a transfixion pin in the comminuted os calcis because of the danger of the development of infection or an osteitis, but these complications have not been encountered in the experience of the writer.



Fig. 3. a, left. Case 6 N. W. Comminuted fracture of the os calcis involving the posterior articular facet. Obliteration of the tuberosity-joint angle. b, The foot in

a plaster cast following reduction by the traction method. Note the restoration of the normal tuberosity-joint angle in this case.

Following reduction, it has been the custom at our clinic to continue traction with the leg on a Braun splint for about 3 months. Upon the removal of the traction, a light walking plaster cast is applied with pressure pads under the malleoli, and worn for about 6 weeks. A shoe with an outer upright brace is then used for protection. This method has been used to maintain reduction, in preference to a plaster cast with the pins incorporated, which permits early walking, for two reasons. A great deal of damage to the tissues, extensive hemorrhage, and swelling are associated with these fractures. It is the writer's opinion that the foot more quickly and more surely returns to normal when it is kept elevated and at rest during the first few months of treatment. Then, too, when a plaster cast is applied soon after reduction it becomes loose as the swelling subsides, allowing deformity to recur.

One of the problems in treatment is the atrophy of the tarsal bones from prolonged disuse, which causes the foot to be sore and painful when weight-bearing is started. Such atrophy is easily overcome if the patient cooperates and uses the foot.

#### REVIEW OF 22 CASES TREATED BY THE BOEHLER METHOD

During the past decade, traction has been used exclusively in our clinic as the method of treating the troublesome squash-type of fracture. The series of 22 cases includes only those cases in which at least 1 year has elapsed from the time of treatment, and in which it has been possible to investigate the end-result. Eleven of these cases were analyzed in a report published previously (8), but these patients have again been examined, and the findings correlated with those of the new series.

All except one of the patients were males, and the majority of them were between 30 and 50 years of age. The fractures had been the result of a fall from a height while the men were at their work as carpenters, telephone repair men, construction men, or laborers. All the fractures sustained were comminuted into the subastragalar joint, with disruption of the articular surfaces, telescoping of the fragments, and lateral bulging below the external malleolus. Reduction was carried out within 4 days of the injury in all cases except one, which was complicated by shock.





Fig. 4. a, left. Case 10 S. M. Comminuted fracture of the os calcis with the posterior articular facet crushed into the body of the bone, displacement of the forward fragment

with the anterior facet, and loss of the tuberosity joint angle. b, Reduction by the traction method, showing the tuberosity joint angle slightly overcorrected.

The 22 patients were examined at periods varying from 1 to 9 years after treatment. The postoperative periods may be summarized as follows: 1 year, 2 cases; 2 years, 1 case; 3 years, 1 case; 4 years, 4 cases; 5 years, 4 cases; 6 years, 3 cases; 7 years, 1 case; 8 years, 2 cases; 9 years, 4 cases.

Evaluation of the end-results on the basis of the recovery of a comfortable, weight-bearing, and functional joint that allows the patient to return to his former occupation showed uniformly good results. Nineteen of the 22

patients returned to their accustomed employment, and in this group were carpenters, heavy construction workers, laborers, and telephone repair men. Four bilateral cases were in this group. Work was resumed in most cases within a period of from 5 to 9 months after the fracture. There is, of course, the psychological factor to be considered in estimating the period of incapacity in cases that involve compensation.

These patients walked without a limp, and they experienced little discomfort, even after



Fig. 5. a, left. Case 5 D. R. Comminuted fracture of the os calcis with marked upward displacement of the entire posterior fragment. b, Roentgenogram taken 4 years, 9

months after reduction by the traction method. Note correction of upward displacement of posterior fragment and restoration of normal tuberosity joint angle.

hard work. Seven patients complained that the foot felt tired after prolonged standing; 1 patient experienced pain when walking on uneven ground; 1 complained of pain in stormy weather; and 1, of stiffness in the morning. The only residual disability was a loss of motion in eversion and inversion from one-third to one-half, but this restriction in itself was not disabling. Two patients had a slight lateral thickening below the external malleolus.

The roentgenograms at the time of the final examination showed that the plane of the joint surface had been restored to normal, and in only 2 cases was there any thickening below the external malleolus. In several roentgenograms there were changes at the subastragalar joint that were suggestive of a fibrous ankylosis, but such findings are to be expected in these severe fractures in which the articular surfaces are destroyed. Illustrative roentgenograms of 3 cases taken before and after reduction are seen in Figures 3, 4, and 5.

There were 3 poor results. One of the patients was a carpenter who sustained a bilateral fracture, and that on the right foot was treated by the traction method. One year after the fracture, an arthrodesis was necessary to relieve the painful arthritis. The second patient is now suffering from an arthritis involving both the ankle and subastragalar joints, and the third patient complains of constant pain and fatigue. In these 3 cases both inversion and eversion are limited to approximately the same degree as in the cases with good end-results. In none of the 3 cases is there any lateral bulging of the os calcis.

## SUMMARY

The difficult problem of restoring perfect function in the squash-type of fracture with disruption of the subastragalar joint is discussed.

Of the present-day methods of treatment, the Boehler traction method is generally recognized as the most satisfactory. By this method the plane of the joint surfaces may be restored to normal, and the lateral deformity corrected. Uniformly good results may be expected in the majority of cases in which the traction method is used, as based upon the criterion of the recovery of a comfortable, weight-bearing, and functional foot and fitness to resume the accustomed work. The only permanent disability is a limitation of the eversion and inversion of the foot, which constitutes no handicap.

A survey of 22 cases treated by the Boehler method is presented. Nineteen of the patients secured good results and returned to their former occupations.

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# PRINCIPLES WHICH GOVERN THE EXTENT OF GASTRIC RESECTION FOR DUODENAL ULCER

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THE basic principles upon which the philosophy of gastric resection in certain cases of duodenal ulcer is founded are today generally accepted as entirely sound, and partial gastrectomy has attained a status in the treatment of this surgical disease which may be sustained and enhanced by the judicious selection of cases wherein it is justifiably applicable in accordance with its objectives.

As the limitation of indications for surgical intervention in duodenal ulcer has been more closely drawn during recent years, so more frequently have the purposes of an operation been most adequately served through excision of the ulcer. It is true that an ulcer in the anterior wall of the duodenum can be excised by simple conservative procedures and that an ulcer in the posterior wall of the duodenum can often be removed through transduodenal and other relatively conservative operations. However, by this time experience has proved that the incidence of recurrence of ulcer has been high following such conservative operations. Gastric resection provides a method for excision of the ulcer and for the control of gastric acidity and gastric secretion not alone through neutralization and dilution by duodenal or jejunal content but through quantitative reduction of gastric acidity consequent upon the removal of acid-secreting gastric mucosa. It may be stated then that the purposes of gastric resection in certain cases of duodenal ulcer are either excision of the ulcer or quantitative reduction of gastric acidity; but in performing partial gastrectomy both objectives are usually served.

Experience has by this time established the idea that in the bleeding duodenal ulcer, in the penetrating ulcer, and in the ulcer that has recurred following the simple closure of an acute perforation, the purposes of surgical interven-

tion are usually best served through performing partial gastrectomy. By this time everyone is in accord with the idea that recurring hemorrhage from an ulcer usually can be permanently controlled only through excision of the bleeding lesion. The futility of any surgical procedure for the control of bleeding which does not include excision of the bleeding ulcer has been observed so often that one may justifiably say that unless the surgeon is competent and is prepared to excise the ulcer in one way or another, surgical intervention should not be contemplated. Experience has by this time proved that usually a bleeding ulcer can be excised most advantageously through performing partial gastrectomy. Many bleeding duodenal ulcers are situated on the posterior wall of the duodenum, and adequate access to this area to facilitate excision of the ulcer-bearing portion of the duodenum is often gained only after transection of the stomach at some level proximal to the pylorus (Fig. 1).

The penetrating ulcer of the duodenum, particularly the ulcer in the posterior wall in which protective perforation has occurred with subsequent penetration of the pancreas, presents technical problems in its excision, the satisfactory solution of which in many instances is found only through transection of the stomach with removal of the distal portion thereof and the first portion of the duodenum to a level just below the ulcer (Fig. 2). Similar problems are not infrequently encountered when recurrence of an ulcer following simple closure of an acute perforation requires subsequent surgical consideration and the solution of these is likewise at times to be found only through removal of a part of the stomach. It is not to be inferred when partial gastrectomy is performed for duodenal ulcer that the ulcer-bearing area of the duodenum should always be included in the resection. There are instances in which the resection limited distally by the pylorus will suffice and in certain other

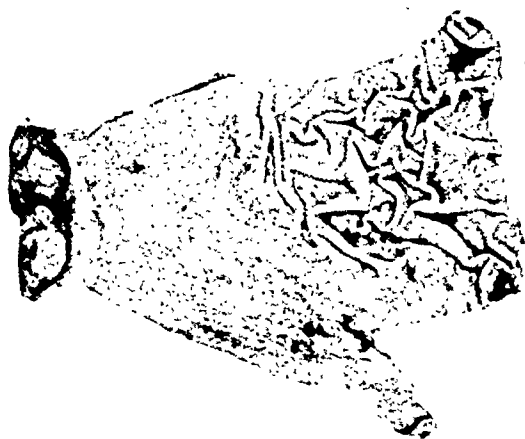


Fig. 1. Inclusion of the bleeding ulcer-bearing portion of the duodenum in the hemigastrectomy.



Fig. 2. Inclusion in the hemigastrectomy of that portion of the duodenum with a posterior penetrating ulcer.

instances the added hazard of excising a penetrating ulcer in the presence of extensive inflammatory reaction is not justified. However, failure to include an actively bleeding duodenal ulcer within the scope of the resection is a serious compromise of the primary purpose of an operation for this complication.

Failure to control gastric acidity adequately through dilution and neutralization by the conservative operations has provided the impetus for quantitative reduction of gastric acidity and gastric secretion through removal of acid-secreting gastric mucosa by partial gastrectomy. Through partial gastrectomy acid-secreting gastric mucosa in varying amounts may be removed and through restoration of gastrointestinal continuity by gastrojejunal anastomosis the jejunal content becomes available for its additional diluent and neutralizing effect upon gastric acids.

The magnitude of partial gastrectomy for duodenal ulcer as pertains to the amount of stomach which it is advisable to remove is variable and is subject to many factors. The terms partial gastrectomy, subtotal gastrectomy, and gastric resection imply removal of a circumferential portion of the stomach without designation of the amount of stomach which is removed in the resection. Not until qualifying terms are universally adopted to designate the amount of stomach that is removed in the operation of partial gastrectomy can comparative results be determined in terms of the extent of the resection. I have suggested that removal of the pyloric half of the stomach be designated as hemigastrectomy and that the various other magnitudes of gastric resection be designated in terms of thirds, quarters, fifths, et cetera (Fig. 3). Wangenstein has designated the amount of

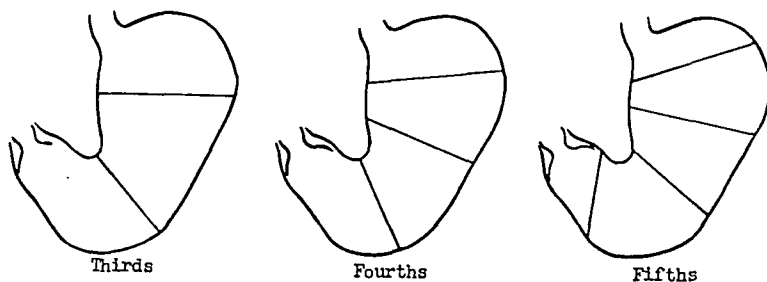


Fig. 3. Designation of the extent of gastric resection.

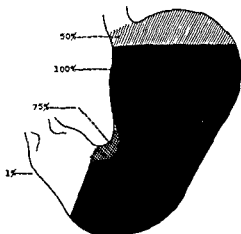


Fig. 4 Distribution of the parietal cells in the gastric glands according to Berger. In the body and fundus of the stomach considerable uniformity exists in the maximum number of parietal cells, in the cross hatched area at the lesser curvature angle the number of parietal cells in the gastric glands is about 75 per cent of that in the fundus of the stomach, in the lightly shaded area at the cardiac portion of the stomach about 50 per cent, and in the unshaded pyloric antrum about 1 per cent

stomach removed in terms of the number of square centimeters of serosal surface.

In the quantitative reduction of gastric secretion and gastric acidity by gastric resection two important questions arise: (1) How much shall the gastric secretion and gastric acidity be quantitatively reduced? (2) How much of the stomach shall be removed to provide the desired reduction? These questions, of course, have to do with the problem of recurrent ulcer following partial gastrectomy. It is known that an anastomotic or jejunal ulcer does develop in a small percentage of cases following gastric resection for duodenal ulcer. Heuer's collective review of a large series of cases revealed an incidence of anastomotic or jejunal ulcer following partial gastrectomy in 0.6 to 6 per cent of the cases with an average incidence of 1.9 per cent. All manner of resections and the various methods of restoring gastrointestinal continuity were included in this review, but no analysis of the incidence of recurrent ulcer in relation to the amount of stomach removed or the types of anastomotic procedures which were employed was possible.

There are those whose enthusiasm for quantitative reduction of gastric acidity has led

them to extend the operation of gastric resection for duodenal ulcer to the point of establishing constant achlorhydria to histamine stimulation. Wangensteen has said that operations which fail to afford real promise of achlorhydria leave too much to chance and hold out too great a risk of gastrojejunal or recurring ulcer to stamp them as satisfactory operations to be invoked frequently for the surgical relief of ulcer. He likewise has said that to procure achlorhydria with a high degree of regularity it is necessary to sacrifice 66 to 80 per cent of the gastric tissue.

One may not discuss the problems pertaining to the extent of gastric resection without at least brief reference to the structure of the gastric mucosa and the functions of the various constituents of that structure. Three types of glands are present in the stomach of man; and while they are designated as fundic, pyloric, and cardiac, each group is characterized by certain cellular content and secretory product. Bensley recognized only two types of glands: (1) the gastric glands proper which occupy the proximal two-thirds of the stomach and whose function in general is to produce the active elements of gastric secretion, and (2) the pyloric glands which occupy the distal third of the stomach, and whose function is mainly the production of mucus. By this time the individual contribution to gastric secretion of each of the several types of cells comprising the gastric glands is fairly well understood, but the mechanism by which the secretions are produced remains mysterious. While, in general, several different types of cells constitute the gastric glands, certain ones are predominant in each of the three divisions of the stomach. Whatever the mechanism may be by which hydrochloric acid is formed it is generally agreed that the parietal cells in the gastric glands are largely concerned and that the degree of gastric acidity is dependent upon them. They are present in all of the gastric glands, but are most numerous in the glands of the body and fundus of the stomach. Berger, in 1933, showed that in the normal stomach the parietal cells are most numerous with quite consistent uniformity throughout the body of the stomach and that the parietal cells are approximately 75 per cent, 50 per

cent, and 1 per cent as numerous in the gastric glands at the lesser curvature angle, at the cardia and at the pyloric antrum, respectively, as in the glands of the fundus or body of the stomach (Fig. 4).

If one may presume that the preoperative degree of acidity can be reduced proportionately to the amount of parietal cell content of the stomach which is removed by gastric resection, it remains to decide upon what degree of postoperative acidity one wishes to attain in accordance with one's own ideas pertaining to the relationship of the degree of gastric acidity to recurrent gastrojejunal or jejunal ulcer and thereby determine the extent of the gastric resection. If one subscribes to the idea that achlorhydria to histamine stimulation is necessary to provide maximum assurance against recurrent ulcer and that there are no deterrents to a constant achlorhydria, he will of necessity sacrifice 65 to 80 per cent of the gastric mucosa. To sacrifice that amount of gastric structure amounts to practically total loss of gastric function and from a functional standpoint is equivalent to total gastrectomy, for the remaining fragment of stomach no longer serves as a receptacle but serves only as a corridor from the esophagus to the jejunum. It must be carried in mind that constant achlorhydria is not usually maintained without subjective manifestations, and one needs only to retain under observation cases in which three-quarters or four-fifths gastric resections have resulted in constant achlorhydria without recurrence of ulcer to encounter the new problems that have entered the picture as the result of total loss of gastric function. On the other hand, if one can subscribe to the idea that gastric resection of a lesser extent, with preservation of a low degree of acidity will provide reasonable assurance against recurrent anastomotic or jejunal ulcer, satisfactory gastric function can be maintained and the sequelae of constant achlorhydria can be obviated. Or to state the matter otherwise, considerable data have accumulated which strongly support the idea that removal of not more than half of the stomach—hemigastrectomy—provides a reasonable assurance against a subsequent anastomotic or jejunal ulcer, maintains a reduced gastric acidity, and

preserves satisfactory gastric function. We also have accumulated data which support the idea that recurrent anastomotic or jejunal ulcer has for the most part in the past developed in those cases in which either pylorotomy, pyloric one-quarter resection or one-third resection has been performed. In my own work I have observed on several occasions such recurrences in cases in which I had previously performed limited gastric resection. On the other hand, I have not observed what might be clinically or roentgenologically suspected as a recurrent anastomotic or jejunal ulcer in which the extent of the gastric resection for duodenal ulcer had been designated as hemigastrectomy.

The degree of gastric acidity is extremely variable, and only through repeated determinations may one approximate the probable average acid curve. From the practical viewpoint, false values are too often obtained upon which the extent of the resection may be predicated and upon which the postoperative results are determined in terms of the degree to which the acids have been quantitatively reduced when the preoperative and the postoperative curves of the gastric acids are plotted after histamine stimulation.

In performing partial gastrectomy for the purpose of quantitatively reducing the gastric acidity one should remain mindful of the fact that dilution and neutralization through gastrojejunal anastomosis operate in conjunction with quantitative reduction in the control of gastric acidity. In other words, the reduction of gastric acidity following gastric resection and gastrojejunal anastomosis is brought about not alone through removal of acid-secreting gastric mucosa, but also through dilution and neutralization by jejunal content, and since diluent and neutralizing material is thereby made available, the quantitative reduction of gastric acidity may be conservative instead of radical to achieve the approximate desired postoperative acid values.

It is my opinion that postoperative achlorhydria not only is not necessary to afford—if not the maximal assurance—at least reasonable assurance against recurrent ulcer but that postoperative achlorhydria is highly undesirable. My own experience with gastric resec-

tion in certain cases of duodenal ulcer has provided me with data which strongly support the thesis that postoperative reduction to approximately one-half of the preoperative degree of acidity provides a reasonable degree of assurance that an anastomotic or jejunal ulcer is a remote possibility. In accordance with this line of reasoning it has been my policy for the most part to confine the magnitude or extent of gastric resection in duodenal ulcer to the pyloric half of the stomach, including the lesser curvature angle of the stomach (hemigastrectomy) and usually the ulcer-bearing portion of the duodenum, resorting to slightly higher resection only in those cases in which the preoperative total acids exceed 100.

It is conceded, even though that has as yet not been my experience, that one may occasionally undershoot the target when performing hemigastrectomy for duodenal ulcer and that an anastomotic or jejunal ulcer may occasionally follow resection of that extent. However, to aim at removal of 75 to 80 per cent of the gastric structure with the sacrifice of most if not all of gastric function in all cases for purposes of obviating the development of an occasional anastomotic or jejunal ulcer hardly seems justified. Such an approach to the problem of the cure of duodenal ulcer is quite analogous to the questionable thesis of total thyroidectomy in the treatment of hyperthyroidism whereby the clinical manifestations and problems of hyperthyroidism are exchanged for those of myxedema.

The results of partial gastrectomy must be analyzed at their full value not only as pertains to the curability of the ulcer, but also in terms of nutritional changes and deficiency states and of the physiological and biochemical processes in the organism as a whole as they are influenced by the magnitude or the extent of the gastric resection. The philosophy of gastric resection in duodenal ulcer has little in common with the principles upon which the rationale of gastric resection and total gastrectomy is founded in the treatment of malignant disease of the stomach. The very nature of the latter disease entirely justifies extensive gastric resection with sacrifice of much and at times all of the gastric structure and the loss of gastric function even though the sequelae of loss of gastric function subsequently become manifested. The evidence is far from conclusive that the curability of benign duodenal ulcer is dependent upon similarly radical gastric resection, and that in order that cure of the ulcer may be achieved the sequelae of major, if not total, loss of gastric function must be accepted.

Through the future universal adoption of one method or another by which the extent of gastric resection may be designated in terms of the amount of stomach which is resected, opportunity may be provided for analysis of the results of the various magnitudes and extents of gastric resection, not only as pertains to the curability of duodenal ulcer but as pertains to the organism as a whole

# THE UTERINE CONTRACTIONS OF LATE PREGNANCY AND THEIR RELATION TO THE DURATION OF LABOR

A Study of 129 Patients with the Lóránd Tocograph

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THE present report is one in a series dealing with the contractions of the uterus which occur during pregnancy.

The first study concerned simply the magnitude of the contractions which take place during the last 2 months, and the influence of advancing pregnancy upon it (2). The second contribution dealt with the occurrence of contractions early in pregnancy and its relation to the duration of labor (3). The latter investigation indicated that few uteri contract to any extent prior to the ninth lunar month and that patients exhibiting such early activity experience significantly short labors. It also showed that the mere presence of contractions after the beginning of the ninth lunar month is of no assistance in predicting the duration of the labor.

The present investigation, like the first one, deals with the magnitude of the contractions which occur during the ninth and tenth lunar months. It was undertaken, however, in order to find out whether knowledge of this characteristic could be employed as an aid in predicting the kind of activity which would be met with at the time of labor. For this reason it was considered necessary to study few records of many (129) patients rather than many records of a few (5) individuals (2).

## MATERIALS AND METHODS

The present observations were made between August 1, 1938, and September 16, 1940, upon patients attending the Maternity Department of the Hospital of the University of Pennsylvania and ones living at the Sheltering Arms Home. All of these women had single pregnancies; all fetal presentations were cephalic, and all deliveries but one were vagi-

nal. No patient exhibited any evidence of cephalopelvic disproportion. The infants weighed between 2,500 and 4,000 grams at birth.

Uterine contractions were recorded with the latest model Lóránd tocograph, shown in Fig. 1 (1). Each patient supplied a single tocographic record made at some time during the 56 days prior to the onset of labor. The recording period in each instance lasted a minimum of 20 minutes. The tocograph supplies a permanent record which makes it possible to measure five characteristics of uterine activity: (a) the hardness or tension of the uterine wall, and the (b) frequency, (c) rhythmicity of occurrence of the intermittent contractions, (d) their strength, and (e) duration.

Uterine tension is a characteristic which it is impossible to measure absolutely by external hysterography. Its relative degree, however, can be expressed in terms of the displacement of the writing pen of the tocograph from its "at rest" position, which occurs as the machine is being placed upon the abdomen of the patient. If the uterus is relatively soft the recording button on the bottom of the tocograph sinks into the abdominal wall and the writing point is not displaced, but if the uterus is hard or tense, the button is forced into the tocograph, in proportion to the tenseness, thus altering the position of the writing pen. The tension is expressed in terms of millimeters of displacement.

The frequency of contractions is expressed as the number per hour.

The rhythmicity of occurrence of contractions is based upon the time interval between the start of one wave and that of the next, and is expressed as the coefficient of variation.

The strength of contraction is measured in terms of the height of the contraction wave and is expressed in millimeters.

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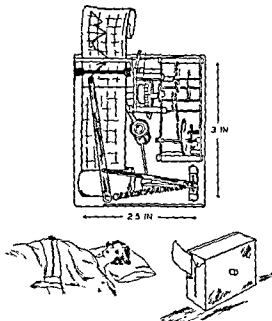


Fig. 1. Latest model Lóránd tocograph, interior and exterior views and in position for recording. Movement of recording button, projecting 0.5 centimeter from bottom of tocograph, is magnified 5 times by writing pen. This instrument is smaller and simpler in construction than model shown in earlier report (2).

The duration of contraction is measured in terms of the length of the contraction wave, and is expressed in seconds.

The magnitude of any characteristic of the uterine contractions of an individual is based upon the measurements of five consecutive waves.

TABLE I.—MEASUREMENTS OF UTERINE TENSION AND CONTRACTIONS DURING 9TH AND 10TH LUNAR MONTHS OF PREGNANCY

	Characteristic				
	Tension*	Contraction wave**			
		Frequency	Rhythm	Height	Duration
	mm	per hr	c of v	mm	seconds
Minimum	0.0	1.0	0.013	0.2	11
Maximum	9.6	84.0	1.017	46.8	516
Mean	$1.6 \pm 1.0$	$10.1 \pm 13.1$	$1.04 \pm .116$	$3.4 \pm 5.1$	$80 \pm 74$

\*Based upon 120 tracings

\*\*Based upon 99 tracings showing contractions

c of v = Coefficient of variation

Note wide spread between minimum and maximum values and large standard deviation of all means.

TABLE II.—INFLUENCE OF DURATION OF PREGNANCY UPON UTERINE TENSION AND CONTRACTIONS

Duration of pregnancy was	Patients					
	No	Mean tension* mm	Characteristic			
			Mean contraction wave**			
			Frequency no/hr	Rhythm c of v	Height mm	Duration seconds
33-34 inc	3	1.0	14.5	.260	3.6	77
35-36 inc	12	1.7	4.4	.115	1.8	80
37-38 inc	35	1.2	10.2	.126	1.2	31
39-40 inc	75	1.0	10.2	.187	4.8	101

\*Based upon 120 tracings

\*\*Based upon 99 tracings showing contractions

c of v = Coefficient of variation

As pregnancy advances note: (a) progressive increase in tension, (b) stabilization of the frequency of contractions during last month, (c) unusual increase in the height (strength) and duration of the contraction waves during the 39-40 week period, and low values for these measurements during the 37-38 week period.

## RESULTS

Of 129 patients, 71 were white, 58 colored; 52 were primigravidae, 87 multigravidae.

**Distribution of measurable characteristics.** Tension was measured in 129 tracings, the height, duration, and frequency of contraction waves in the 99 tracings in which waves were observed, and rhythm only in those tracings which recorded three or more contractions.

**Summary of all measurements.** Minimum, maximum, and mean values of tension and

TABLE III.—INFLUENCE OF DURATION OF PREGNANCY UPON DISTRIBUTION OF PATIENTS HAVING NO UTERINE CONTRACTIONS

Duration of pregnancy wks	Patients			
	No	%	With no contractions	
			No	%
33-34 inc	3	1.3	0	0.0
35-36 inc	12	9.3	4	11.9
37-38 inc	35	27.9	16	15.1
39-40 inc	75	60.5	0	0.0
Total	120	100.0	20	100.0

Note that an absence of contractions was observed most frequently in tracings secured during the 37-38 week period, where contractions of small magnitude were observed (Figure 2).

TABLE IV.—INFLUENCE OF PARITY UPON UTERINE TENSION AND CONTRACTIONS

PARIETY UPON UTERINE TENSION AND CONTRACTIONS							
Parity	No.	Patients					Mean duration of labor hrs.
		Mean tension mm.	Characteristic				
			Mean contraction wave*				
			Frequency no./hr.	Rhythm c. of v.	Height mm.	Duration seconds	
Primiparas	42	2.0 ± 2.0	20.2 ± 18.8	.310 ± .217	3.2 ± 2.1	103 ± 95	16.0 ± 10.1
Multiparas	87	1.4 ± 2.0	10.3 ± 13.0	.290 ± .238	4.5 ± 3.0	106 ± 60	8.9 ± 7.4

\*Measurements of primiparas based upon 34 tracings showing contractions.  
Measurements of multiparas based upon 64 tracings showing contractions.  
c. of v.=coefficient of variation.

Note: (a) difference in mean duration of labor between primiparas and multiparas is significant.

\*Measurements of primiparas based upon 34 tracings showing contractions.  
Measurements of multiparas based upon 64 tracings showing contractions.  
c. of v.=coefficient of variation.

Note: (a) difference in mean duration of labor, (b) the lower frequency of contractions, and their greater rhythmicity, strength and duration in the multiparas.

contractions appear in Table I. These data attest to the wide individual variation of all measurements.

*Influence of duration of pregnancy upon uterine tension and contractions.* The mean values of the contraction waves are shown in Table II, arranged according to the duration of pregnancy at the time that they were recorded. Tension increased progressively as pregnancy advanced. The frequency of contractions appeared to become stabilized during the last month, although there was no significant improvement in rhythmicity.

The height and duration of the contraction waves were greatest during the 2 weeks immediately before labor, but were unusually small during the 37 to 38 week period.

*Influence of duration of pregnancy upon distribution of tracings registering no uterine contractions.* Thirty-one tracings registered no contractions. Table III records their distribution according to the time in pregnancy that they were secured. Although the majority of all tracings were made during the 39 to 40 week period, tracings showing no contractions appeared most often in the preceding two week period. It is significant that the presence of low grade contractions (Table II) was observed according to the time in pregnancy that they were secured.

TABLE VI.—INFLUENCE OF FREQUENCY OF CONTRACTIONS UPON DURATION OF LABOR

Contractions per hour	Patients	
	No.	Mean duration of labor in hours
Reported	129	11.2 ± 9.0
0.0*	31	10.3 ± 6.8
0.1-9.9	56	10.3 ± 9.8
10.0 plus	42	13.2 ± 8.8

\*No contractions recorded.

Note that the short labors were associated with an absence of contractions, or with ones of low frequency.

TABLE VII.—INFLUENCE OF RHYTHMICITY OF CONTRACTIONS UPON DURATION OF LABOR

Coefficient of variation	Patients	
	No.	Mean duration of labor in hours
Reported	129	11.2 ± 9.0
0.000*	57	9.7 ± 5.5
0.001-0.299	45	11.1 ± 10.1
0.300-0.599	19	14.0 ± 10.5
0.600 plus	8	16.2 ± 7.2

\*Number of contractions insufficient for computing coefficient of variation.

Note that the shortest labors were associated with the lowest coefficient of variation.

TABLE V.—INFLUENCE OF UTERINE WALL TENSION UPON DURATION OF LABOR

Tension in millimeters	Patients	
	No.	Mean duration of labor in hours
Reported	129	11.2 ± 9.0
0.0*	63	11.5 ± 8.7
0.1-4.9	52	10.6 ± 7.6
5.0-9.9	14	12.2 ± 13.5

\*No increase in tension observed.

Note that the highest degree of tension was followed by the longest labors.

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TABLE VIII.—INFLUENCE OF STRENGTH OF CONTRACTIONS UPON DURATION OF LABOR

Wave height in millimeters	Patients	
	No	Mean duration of labor in hours
Reported	129	11 $\pm$ 9.0
0.0*	31	10 $\pm$ 6.0
0.1-4.9	64	11 $\pm$ 8.6
5.0-9.9	31	11 $\pm$ 17.9
10.0-14.9	3	10 $\pm$ 15.3

\*No contractions recorded

Note shortness of labors in patients experiencing no contractions, and the very short labors in those having the strongest contractions

TABLE IX.—INFLUENCE OF DURATION OF CONTRACTIONS UPON DURATION OF LABOR

Duration of contraction in seconds	Patients	
	No	Mean duration of labor in hours
Reported	129	11 $\pm$ 9.0
0.0*	31	10 $\pm$ 6.0
0.1-29.9	7	17 $\pm$ 3.0
30.0-59.9	20	11 $\pm$ 6.6
60.0-89.9	23	13 $\pm$ 8.2
90.0-119.9	18	9 $\pm$ 8.8
120.0 plus	10	9 $\pm$ 8.3

\*No contractions recorded

Note shortening of labors as the duration of contractions increases

served at the same time. Perhaps this drop in activity may have an endocrine basis.

*Influence of parity upon contractions.* The magnitude of the contractions of the primiparas (primigravidas) is compared with that of the multiparas in Table IV. The latter exhibited shorter labors which were preceded by: (a) lower tension, (b) less frequent contractions; these were (c) more rhythmic, (d) stronger and (e) longer than those of the multiparas. The most obvious difference was in contraction frequency.

*Influence of individual contraction characteristics upon duration of labor.* The influence of the contraction characteristics, considered separately, upon the duration of labor appears in Tables V to IX. The standard deviations of

all measurements are large, indicating the wide variability in individual characteristics. The data are such that no significant differences are observed between classes in any one table. In spite of this fact certain trends appear: The shortest labors occurred under the following conditions: (a) a low uterine tension, and (b) when the contractions were infrequent, rhythmic, strong, and of long duration.

*Contraction measurements of patients having different length labors.* Contraction measurements of patients having labors of less than 8 hours are compared with those of women who had labors lasting more than 16 hours, in Table X. The shorter labors were preceded by (a) a lower contraction frequency, (b) greater

TABLE X.—MEASUREMENTS OF UTERINE TENSION AND CONTRACTIONS IN RELATION TO DURATION OF LABOR

Labors	Patients					
	No	Mean tension mm	Characteristic			
			Mean contraction wave*			
			Frequency no/hr	Rhythm c of v	Height mm	Duration seconds
All	129	16 $\pm$ 1.9	10 $\pm$ 13.2	165 $\pm$ 22.6	3 $\pm$ 5.1	80 $\pm$ 7.4
Under 8 hours	55	10 $\pm$ 2.3	9 $\pm$ 8.7	275 $\pm$ 30.2	4 $\pm$ 3.0	110 $\pm$ 29.0
Over 16 hours	23	18 $\pm$ 1.8	13 $\pm$ 10.0	108 $\pm$ 24.2	3 $\pm$ 2.2	88 $\pm$ 31

\*Measurements of "under 8 hours" group based upon 42 tracings showing contractions  
 \*Measurements of "over 16 hours" group based upon 19 tracings showing contractions  
 c of v = Coefficient of variation.

Mean values of the contraction measurements of patients having labors of more than 16 hours compared with those having labors of less than 8 hours' duration. Note that the patients having shorter labors experience (a) a low contraction frequency, (b) greater rhythmicity in the occurrence of contractions, (c) stronger and (d) longer contractions than those having longer labors

rhythmicity, (c) stronger and (d) longer contractions, and (e) greater tension than were the longer labors.

#### OBSERVATIONS

The patients supplying the present observations fall into two groups: those who experienced contractions and those who did not. The latter individuals had shorter labors than the average. It would follow from this that the absence of contractions is no sign that the labor will be long.

The contractions exhibited a wide variation in their measurements from individual to individual. This was so great that it would seem difficult to predict the length of any given patient's labor on the basis of a single tographic record. In spite of this variability there did exist a relation between the nature of the uterine motility during the ninth and tenth months of pregnancy and the length of labor.

Tension was found to have no value in predicting the duration of the labor, whereas knowledge of the contractions was a help. The short labor was usually preceded by contractions which were found to be especially infrequent, rhythmic, long and strong.

Certain other features of the contractions, which do not lend themselves readily to statistical treatment, also indicate that a satisfactory type of labor can be expected. Contractions which rise slowly to a maximum and fall away at the same rate, almost regardless of their strength, prognosticate a more efficient kind of activity during labor than ones which rise and fall quickly. This may be only another way of saying that a long contraction is better than a short one. Certain patients present a contraction pattern of such a kind that it is possible to superimpose one wave and its following valley upon an adjacent one. Such patients may be said to exhibit a nearly perfect rhythmicity in respect to all characteristics of their contraction waves, e. g., size, shape, duration, frequency, and rhythmicity. These women experience short labors. The

short labor can be predicted more upon the quality of the contractions than upon their size. Rhythmicity in all characteristics of the contraction appears to be the ideal to be attained if the quality of the labor is to be optimum.

#### SUMMARY AND CONCLUSIONS

1. The uterine motility of 129 patients was recorded with a Lóránd tograph during the ninth and tenth lunar months of pregnancy.

2. Measurements of tension, and of frequency, rhythmicity of occurrence, strength and duration of the contractions were correlated with: (a) time of recording, (b) parity, and (c) duration of labor.

3. Measurements of all characteristics of motility exhibited wide individual variations.

4. Advancing pregnancy was associated with: (a) a progressive increase in tension, (b) a tendency for the frequency of contractions to become stabilized during the last month, (c) absence of contractions, and ones of unusually small magnitude during the 37 to 38 week period, (d) exceptionally long, strong contractions during the 39 to 40 week period.

5. Multigravidas and individuals experiencing short labors exhibited contractions during late pregnancy which were: less frequent, more rhythmic in occurrence, stronger and longer in duration than did primigravidas and individuals who had longer labors.

6. From these observations two conclusions seem justified: (a) The duration of labor of a given individual cannot necessarily be predicted from an examination of a single tographic record made at random during the last two lunar months of pregnancy. (b) In general short labors are preceded by a uterine motility which differs from that experienced by individuals who have longer labors.

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# THE INTRAVENOUS USE OF SYNTHETIC VITAMIN K<sub>1</sub>

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THE clinical value of vitamin K is well established. Various substances with vitamin K activity have served to relieve the bleeding tendency associated with prothrombin deficiency in obstructive jaundice, hemorrhagic disease of the newborn, various disorders of the liver, and of the intestinal and biliary tracts.

Since the presence of bile in the intestinal tract is required for the absorption of the vitamin, oral therapy, in cases of complete biliary obstruction or fistula, necessitates the giving of bile salts. Nausea and vomiting, often increased by the ingestion of bile salts, make oral administration uncertain and sometimes impossible.

A method of administering synthetic vitamin K<sub>1</sub> (2-methyl-3-phytyl-1, 4-naphthoquinone—see Fieser, 6) intravenously has been described by three of us (10). The rapidity and prolonged duration of action of single doses of vitamin K<sub>1</sub>, when administered intravenously, exceed those reported by other investigators using drugs with vitamin K activity by oral, intramuscular and intravenous routes. (2, 3, 11, 19, 20, 22). This paper presents the results of further studies of the intravenous use of synthetic vitamin K<sub>1</sub>. It also includes certain data on the effects of the intravenous administration of 2-methyl-1, 4-naphthoquinone and of a water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone.<sup>1</sup>

## METHOD

Through the courtesy of Professor Louis F. Fieser, synthetic vitamin K<sub>1</sub> was obtained for this study. This substance, which is an oil at room temperature, was given intravenously in a colloidal suspension, prepared by dissolving

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<sup>1</sup>Synthesized (8) and kindly supplied by Professor Louis F. Fieser

10 milligrams of the vitamin in 3 cubic centimeters of ethanol and introducing the solution slowly under the surface of 1 liter of a 10 per cent solution of glucose in distilled water, while this was being constantly agitated. The suspension was then autoclaved for 20 minutes at 120 degrees C. The product was slightly opalescent. No change in appearance was noted in ampuls of the suspension which had been stored for 5 months, and the material was found to have retained its activity during this time. Because quinones are altered by sunlight, the solutions were stored in the dark. No untoward reaction followed the use of this material when given intravenously. In a case in which it was not possible to evaluate the effectiveness of the drug, no local reaction followed the administration of the colloidal suspension by claysis. 2-Methyl-1, 4-naphthoquinone was prepared for intravenous use in the same way and was found to be slightly more soluble. Doses of 10 to 20 milligrams of the sodium salt of the sulfuric ester of 2-methyl-1, 4-naphthohydroquinone are readily soluble in 1 cubic centimeter of water.<sup>2</sup>

Prothrombin times were determined by the method of Quick (13). The range for normal adults was 14 to 17.5 seconds when the thromboplastin plasma mixture was brought to 37 degrees C. before the addition of calcium chloride.

## RESULTS

### Obstructive Jaundice

The results in obstructive jaundice are shown in the following case histories.

H R B, No P B B II 562750, a 79 year old man, entered the hospital because of recurrent vomiting and jaundice. He had been well until 8 months before entry when he began to vomit with increasing frequency, although he had no nausea. Two weeks before his entrance into the hospital he became jaundiced; his stools became clay colored, and his urine became dark.

<sup>2</sup>For stability an equal weight of sodium bicarbonate was dissolved in the solution

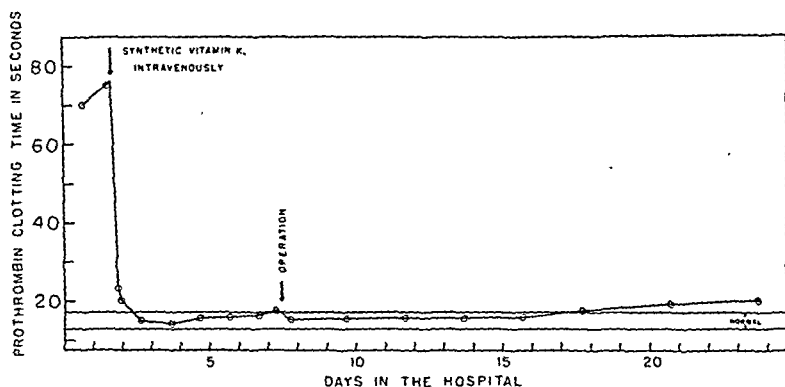


Chart 1. Prothrombin time determinations in case H. R. B., obstructive jaundice.

Examination revealed emaciation and jaundice. There was slight tenderness in the right upper quadrant of the abdomen. The liver dulness extended downward from the fifth interspace, and the edge could be palpated 5 centimeters below the costal margin in the midclavicular line. Laboratory data included: white blood cells, 8,600, with normal differential; stools, clay colored, guaiac positive; urine contained bile; vomitus, dark guaiac positive; icterus index, 125. Bleeding time was 5 minutes; clotting time 5 minutes, 30 seconds; prothrombin time, 70 seconds. There were marked ecchymoses about the needle puncture wounds. The patient was given 10 milligrams of vitamin K<sub>1</sub> intravenously 24 hours after admission. Laparotomy was performed on the seventh hospital day. The liver was found to be studded with metastatic carcinoma arising in the head of the pancreas, and no palliative procedure was possible. There was no unusual bleeding during the operation.

Following laparotomy, the patient continued to vomit. He received all nourishment parenterally. He discharged much bile-stained fluid through the abdominal wound, and the stools remained clay colored. He showed no tendency to bleed. His course was progressively downhill and he died on the twenty-sixth hospital day. Autopsy revealed carcinoma of the head of the pancreas with metastases to liver and mesentery, with obstruction of the common bile duct.

This patient with obstructive jaundice of at least 2 weeks' duration entered with an abnormal prothrombin level which was associated with a bleeding tendency. A single dose of vitamin K<sub>1</sub> produced a marked drop in prothrombin time in 4 hours and a return to normal within 16 hours. He underwent operation 6 days later, with a normal prothrombin level. There was no abnormal bleeding. Although the operation failed to relieve the biliary obstruction, his prothrombin level re-

mained within normal limits for 2 weeks without additional vitamin K. The prothrombin time determinations are recorded in Chart 1.

E. F. C., No. P.B.B.H. s63362, a 52 year old man, entered the hospital because of progressive weight loss and jaundice. During the previous 7 years he had consumed large quantities of alcohol. Six weeks before entry he began to lose his appetite, and 3 weeks before entry he became jaundiced; his stool became clay colored, his urine dark. His nose bled several times during the weeks before admission.

Examination revealed an obese white man with yellow, excoriated skin and icteric sclerae. The abdomen was large. The liver dulness extended down from the fifth interspace and a firm, smooth, non-tender liver could be felt 4 fingers' breadths below the costal margin. The area of splenic dulness was enlarged. Laboratory data included: white blood cells 6,650, with normal differential; icterus index, 74; serum protein 6.0 grams; albumin, 2.3 grams; globulin, 3.7 grams; bromsulphthalein test showed 60 per cent retention at 30 minutes; urine contained albumin and bile; stools were clay colored without bile; bleeding time, 2½ minutes; clotting time, 2 minutes; prothrombin time, 48 seconds.

In the hospital epistaxis continued. There were ecchymoses about the needle puncture wounds. One half-milligram of vitamin K<sub>1</sub> was given intravenously. The nosebleeds stopped. Two days before operation 10 milligrams of vitamin K<sub>1</sub> were given intravenously. Operation, performed on the nineteenth hospital day, revealed marked hepatitis, cirrhosis, and many large and small carcinomatous nodules in the liver. No palliative procedure was possible. There was no abnormal bleeding at operation, and the wound healed well. The postoperative course was one of progressive weakness with jaundice. The urine continued to contain bile. There was no evidence of bile in the stools at any time. There was no recurrence of bleeding and no further vitamin K was given. On the thirty-fifth hospital day he was discharged to a convalescent home.

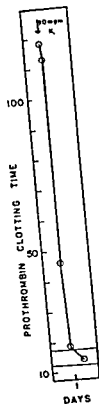


Chart 3

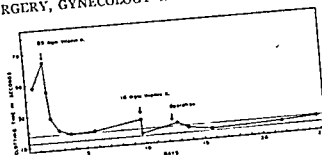


Chart 2

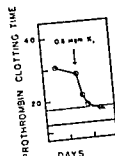


Chart 4

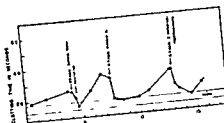


Chart 5

- Chart 2 Prothrombin time determinations in case E. I. C., obstructive jaundice  
 Chart 3 Prothrombin time determinations in case A. K., obstructive jaundice  
 Chart 4 Prothrombin time determinations in case I. B., obstructive jaundice  
 Chart 5 Prothrombin time determinations in case S. C., obstructive jaundice

This patient with obstructive jaundice of at least 3 weeks' duration entered the hospital with an abnormal prothrombin level. The response to 0.5 milligram of vitamin  $K_1$  intravenously is shown in Chart 2. The prothrombin level reached normal 2 days after injection but rose again to 24 seconds in 5 days. The slow response to this dose may have been due in part to the cirrhosis and hepatitis noted at laparotomy.

Following a 10 milligram dose of vitamin  $K_1$  the prothrombin level returned to normal and remained so for at least 15 days, despite the fact that the patient underwent an operation which did not relieve the biliary obstruction.

A. K., No. P. B. H. 1557100, a 70-year-old woman, entered because of nausea and jaundice. Two years before entry she had had painless jaundice, nausea, and fatigue, which subsided after about a month. Except for occasional bouts of nausea, she had been well until 6 weeks before entry when she had a shaking chill followed by vomiting and diarrhea. She

developed jaundice, had tarry stools, and vomited large quantities of coffee ground material. Two days before entry she again had chills with a fever of 102 degrees F., and had several dark bowel movements.

Examination revealed an elderly icteric woman vomiting frequently. There were a few rales at the lung bases and a soft systolic apical murmur. The liver could be percussed 1 finger's breadth below the costal margin. The gall bladder was not felt. Laboratory data included hemoglobin, 55 per cent, red blood cells, 3,300,000, white blood cells, 23,600 with 93 per cent neutrophils, urine contained bile, albumin, acetone, diacetic acid, occasional red blood cells, white blood cells, and hyaline casts. Stools could not be obtained. The vomitus was black, benzidine positive. The icterus index was 80. The prothrombin time was 118 seconds. Ten milligrams of vitamin  $K_1$  was given intravenously. At that time there were ecchymoses about the needle puncture wounds and the patient was vomiting bloody material. She continued to vomit grossly bloody fluid. Her course was progressively downhill and she died 40 hours after entry.

Postmortem examination was performed with the following findings: carcinoma of the ampulla of Vater with obstruction of the common bile duct,

suppurative cholangitis; generalized icterus; biliary hemorrhage and gastrointestinal hemorrhage.

This woman entered the hospital with obstructive jaundice, bleeding, and marked prothrombin deficiency. Although she was moribund on admission and died 40 hours thereafter, the prothrombin time dropped from 118 seconds to 18.5 seconds within 4 hours after a single 10 milligram dose of vitamin K<sub>1</sub> was given. The prothrombin determinations are recorded in Chart 3.

I. B., No. P.B.B.H. 563751, a 70 year old woman, entered the hospital because of jaundice and itching. She had been well until 5 months before entry when she began to lose weight. One month before entry she became jaundiced, had orange urine, and passed pale stools.

Examination revealed jaundice, bleeding excoriations of the skin and liver edge palpable 1 finger's breadth below the costal margin. Laboratory data included: white blood cells 7,600 with 66 per cent neutrophils; urine contained bile and occasional red blood cell; stools, clay colored, guaiac positive; icterus index, 62; non-protein nitrogen 42 milligrams per cent; total serum protein, 6.9 grams. The prothrombin time was 30 seconds. She was given 0.6 milligram of vitamin K<sub>1</sub> intravenously on her third hospital day. Two days later a laparotomy was performed which was attended by no unusual bleeding. The head of the pancreas was found to be markedly enlarged, distorting the duodenum. Cholecystgastrotomy was done. Following the operation the icterus index dropped, the urine became pale, and bile appeared in the stools. She was discharged on the sixteenth hospital day.

This patient with obstructive jaundice of at least 1 month's duration entered with an abnormal prothrombin time. The prothrombin deficiency was corrected within 16 hours by a single dose of only 0.6 milligram of vitamin K<sub>1</sub>. The prothrombin time determinations are recorded in Chart 4. The autoclaved colloidal suspension used in this case had been stored in sealed glass ampuls in the dark, at room temperature, for 5 months before use.

S. C., No. B.I.H. 51382, a 45 year old woman who had had cholecystectomy for cholelithiasis without jaundice 5 months earlier, entered, stating that she had drained large amounts of bile from her wound for a month after operation. After the drainage stopped, she developed increasing jaundice. The stools had remained clay colored in the postoperative period and bile appeared in the urine with the development of jaundice.

Examination disclosed deep icterus and a smooth, firm, non-tender liver, palpable 4 fingers' breadth below the costal margin. The urine contained large

amounts of bile; stool, pale; icterus index, 140; cholesterol, 320; cholesterol esters, 178; non-protein nitrogen, 27; prothrombin time, 19 seconds.

Because of a slowly rising prothrombin time a water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone was given intravenously before operation. At operation the common duct was found to be completely transected and the liver bile was colorless. Anastomosis about a T-tube was accomplished. There was no unusual bleeding during or after the operation. The convalescence was satisfactory and the T-tube drained bile which became golden-brown in color. The icterus index fell; bile disappeared from the urine, and the stools became brown. Because the prothrombin time rose after operation the effect of a minimal dose of vitamin K<sub>1</sub> was investigated and the effect was compared with that of the same small dose of 2-methyl-1, 4-naphthoquinone. The patient was discharged on the seventeenth postoperative day with T-tube remaining in place, draining bile.

This patient with postcholecystectomy jaundice which followed the spontaneous closure of a biliary fistula showed increasing hypoprothrombinemia early in the second postoperative period after reconstruction of the common duct, despite the return of bile to the intestinal tract. Four tenths milligram of vitamin K<sub>1</sub> caused a reduction in the prothrombin time from 31 seconds to 18.5 seconds within 6 hours and maintained the level near normal limits for 2 days. On the other hand, this same dose of 2-methyl-1, 4-naphthoquinone, administered in the same way on a later occasion, required 36 hours for a reduction in clotting time to normal, and the effect was shorter in duration. This was noted in spite of the fact that the patient was putting more bile into her intestinal tract and thus perhaps was absorbing additional vitamin K from her food during the latter period of observation. The effect of a large dose of the water soluble ester of 2-methyl-1, 4-naphthohydroquinone, given before operation was found to be short. The prothrombin time determinations are recorded in Chart 5. The case exemplifies the possibility of postoperative fall in blood prothrombin despite the return of bile to the intestinal tract. This may be related to the failure of production of bile acids by the liver immediately after release of biliary obstruction (15, 16).

The intravenous injection of synthetic vitamin K<sub>1</sub> was effective in the treatment of prothrombin deficiency of obstructive jaundice.



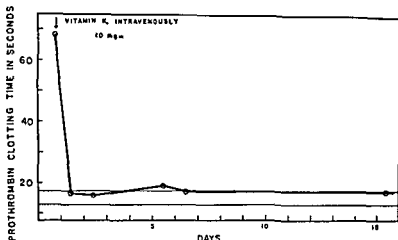


Chart 6 Prothrombin time determinations in case M. L., biliary fistula

Marked drops in prothrombin time were observed within 4 hours after injection, and normal levels were reached within 10 to 16 hours. A 10 milligram dose resulted in the maintenance of a normal prothrombin level for as long as 15 days of unrelieved biliary obstruction. A half milligram dose showed a distinct response which was of short duration. No difficulty occurred in the preparation of these patients for operation and no unusual bleeding accompanied or followed the surgical procedures.

In one case, a small dose (0.5 milligram) of vitamin K<sub>1</sub> gave a better effect than the same dose of 2-methyl-1, 4-naphthoquinone. In this same patient the effect of a large dose (20 milligrams) of a water soluble ester was noted to be shorter than that of the small doses of the quinones. This case study also emphasized the necessity of watching the prothrombin level in the immediate postoperative period, even though the flow of bile has been returned to the intestinal tract.

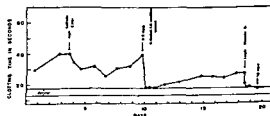


Chart 7 Prothrombin time determinations in case H. M., biliary fistula.

Despite the more frequent occurrence of obstructive jaundice due to calculus, significant prothrombin deficiency was found more often in cases of malignant biliary obstruction.

### Biliary Fistula

The results in biliary fistula are shown in the following cases.

M. L., No. M.G.H. 175730<sup>1</sup>, a 23 year old female underwent cholecystectomy for recurrent attacks of biliary colic of 2 years' duration. At operation chronic cholecystitis with multiple stones was found. After operation bile leakage into the subhepatic space occurred. After this was drained, a total biliary fistula developed. The patient was very ill and vomited frequently. The blood prothrombin level fell markedly within 10 days despite persistent attempts to feed the patient's own bile, bile salts, and vitamin K by mouth and through a stomach tube. The patient was transfused repeatedly. Jejunostomy was done for feeding purposes and at this time bleeding was noted in the peritoneal cavity. In the subsequent 8 months the patient was given her own bile, supplementary bile, and vitamin K preparations through the jejunostomy or by mouth. This period included an unsuccessful attempt to reconstruct the biliary tract.

The present admission occurred 4 months after the latter operation, throughout which period the patient stated that she had continued to take her own bile, as well as commercially available vitamin K preparations, by mouth. There is some question, however, as to how faithfully she had done so. She re-entered the hospital because of the spontaneous development

<sup>1</sup>Acknowledgment is made to the Massachusetts General Hospital for permission to study this case.

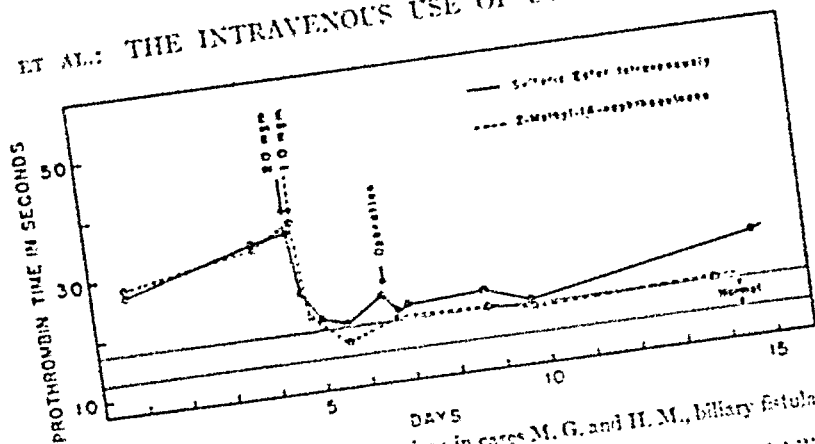


Chart 8. Prothrombin time determinations in cases M. G. and H. M., biliary fistulas.

the ex- done. After operation a total biliary  
The patient vomited repeatedly  
The patient remained. She

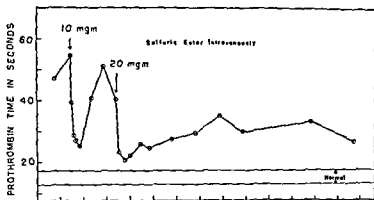


Chart 9 Prothrombin time determinations in case M. G., biliary fistula

to transection of the common duct. At one period in the course of the patient's illness, 10 milligrams of 2-methyl-1, 4-naphthoquinone were given and the course of the prothrombin times shown in Chart 8 may be compared with the effect of a 20 milligram dose of the water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone given to a patient with obstructive jaundice which became converted to a biliary fistula (M. G.). This case afforded an opportunity to compare the efficacy of several antihemorrhagic substances. Small doses were used in order to bring out their differences. Chart 7 shows the effect of 1 milligram of a water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone, of 0.5 milligram of a colloidal suspension of 2-methyl-1, 4-naphthoquinone, and of 1 milligram of vitamin K<sub>1</sub>, given after the second laparotomy. The chart shows the poor effect of the water soluble ester and the marked drop in prothrombin clotting time which reached normal within 24 hours after injection of 0.5 milligram of 2-methyl-1, 4-naphthoquinone. The level remained near normal limits for about 24 hours and then gradually rose again. This may be contrasted with the longer effect of the larger dose given on the previous occasion. The curve of action of 1 milligram of vitamin K<sub>1</sub> was not followed to completion in this case because of the serious bleeding from the common duct which prompted the surgeon to give the patient an additional 10 milligrams of the vitamin. The bleeding stopped after the catheter was removed, and was probably due

to ulceration of the common duct by the catheter.

M. G., No. B.J.H. 22209, a 65 year old white female, entered complaining of right upper quadrant pain associated with nausea and fever of 5 hours' duration. She had had similar attacks in the past year and a half. Examination revealed evidence of marked weight loss, sallow skin, tenderness, spasm, and a palpable mass in the right subcostal region. The icterus index was 4, white blood cells, 24,000, and temperature 102 degrees F. Laparotomy was performed, and a pus filled gall bladder containing many stones was removed. After operation the patient developed bilateral pneumonia. Sulfapyridine therapy was instituted for 4 days with good results. Throughout the postoperative period, biliary drainage from the wound was profuse, and the stools were clay colored. The mercuric chloride test for bile in the stools was consistently negative after the fifth postoperative day. The prothrombin clotting time on the sixth day following operation was 47 seconds. The patient was treated on two occasions with a water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone.

On the twenty-fourth postoperative day, drainage ceased and the patient became increasingly jaundiced. Icterus index rose to 37 and clay colored stools persisted. The prothrombin clotting time had gradually increased and on the twenty fourth day was 34 seconds. She was again treated with the water soluble ester. Two days later an exploratory laparotomy was performed, but the common duct could not be found. She received a blood transfusion. Bilateral pneumonia recurred and again responded to sulfapyridine by the fourth postoperative day. After operation she developed a biliary fistula and clay colored stools which persisted until the fourteenth postoperative day, when biliary drainage ceased and her stools became brown. Four days later she was discharged with an icterus index of 3 and prothrombin clotting time of 20 seconds. The patient was again seen in the out-patient department 2 months

later because of epigastric pain, vomiting, and weakness, and was found to be jaundiced. She refused hospitalization and it was learned that she had died at home on the following day.

This patient with a complete biliary fistula following cholecystectomy was found to have a prolonged prothrombin clotting time on the sixth postoperative day. Both a 10 milligram and a 20 milligram dose of a water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone were given intravenously with the effects shown in Chart 9. Although the drops in prothrombin time were rapid, at no time did they reach normal, and the duration of effect was short. The coexistent pneumonia and sulfapyridine therapy may have played some part in aggravating the prothrombin deficiency. After the patient's fistula had closed spontaneously and she had developed obstructive jaundice, the prothrombin time gradually rose. Another 20 milligram dose of the water soluble ester was given intravenously. The effect of this dose is compared in Chart 8 with the effect of a 10 milligram dose of 2-methyl-1, 4-naphthoquinone given intravenously to patient H. M., with a biliary fistula. Two days after this last dose she underwent an operation which converted the biliary obstruction to a fistula with continuing absence of bile from the intestinal tract for 14 days. Despite this and despite a recurrence of postoperative pneumonia which again was treated by sulfapyridine the effect of this 20 milligram dose of the sulfuric ester was more marked and more prolonged than that of the same dose of the same drug given on an earlier occasion. The caution required in interpreting differences in the effects of drugs given in similar disease states, even in the same patient, is emphasized.

The low blood prothrombin levels of patients with total biliary fistula responded to intravenous vitamin K therapy in much the same way as did those of cases of obstructive jaundice. The characteristic response to vitamin K<sub>1</sub> was shown by M. L. The poorer effects of large doses of the water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone were seen on several occasions in patient M. G. and were compared with the

effects of a similar dose of 2-methyl-1, 4-naphthoquinone given to patient H. M. whose prothrombin deficiency seemed to be of the same order of magnitude.

Total biliary fistula may exist for long periods before the development of prothrombin deficiency, Case H. M. This cannot be predicted, however, because both Case M. G. and Case M. L. showed marked prothrombin deficiency within 10 days after establishment of the fistula. In the former case the acute biliary infection before operation and the pneumonia after operation and sulfapyridine therapy may have contributed to the earlier appearance of hypoprothrombinemia. The latter patient, as well, was acutely ill in the immediate postoperative period. Inability to take adequate nourishment by mouth in the early postoperative period was common to all 3 patients.

### *Hepatitis*

The results in hepatitis are shown in the following cases.

C. S. N., No. P.B.B.H. m57021, a 61 year old woman, entered the hospital because of jaundice. At the age of 21 she had had a transient episode of fever and jaundice. For the past year she had felt tired and had taken increasing amounts of alcohol. During the month before entry she subsisted almost entirely on alcohol and had nausea and anorexia accompanied by progressive jaundice. She became constipated, developed abdominal swelling and passed several clay colored stools. For many years she had had occasional epistaxis. In the last month before entry she had noticed a few drops of blood on her pillow every morning.

Examination revealed an elderly, emaciated white woman, obviously ill. Her skin was hot, dry, jaundiced and excoriated, with a few spider telangiectases. Her abdomen was distended, tympanitic, with a fluid level, and slightly tender in both upper quadrants. The liver dullness extended from the fifth interspace anteriorly on both sides of the chest and the liver was smooth and palpable 2 fingers' breadth below the costal margin in the midclavicular line. The laboratory data were as follows: white blood cells 21,000 with 80 per cent neutrophils; serum protein, 6.5 grams; albumin, 2.1 grams; globulin, 4.4 grams; non-protein nitrogen, 77 milligrams per cent; icterus index, 135. Urine was normal except for the presence of bile. Stools were clay colored. Ascitic fluid was yellow. There were ecchymotic spots about the patient's needle puncture wounds.

She received intravenous glucose and a high caloric diet and seemed to improve for a day or two.

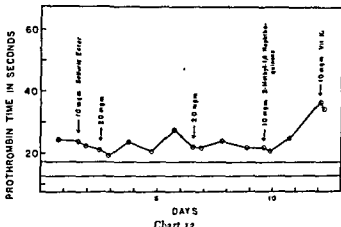
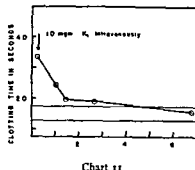
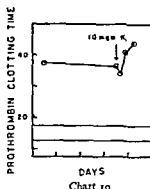


Chart 10 Prothrombin time determinations in case C. S. N., hepatitis.

Chart 11. Prothrombin time determinations in case L. F. D., hepatitis.

Chart 12 Prothrombin time determinations in case S. M., hepatitis.

On the fourth hospital day she became drowsy and jaundice increased. Prothrombin time was 38 seconds. Ten milligrams of vitamin  $K_1$  were given intravenously. The jaundice deepened, the patient lapsed into coma and died on the fifth hospital day.

Autopsy revealed portal cirrhosis of the liver with acute hepatitis and acute suppurative cholangitis. The biliary tracts were not dilated or obstructed. Culture of the liver contained *Clostridium welchii* and *Escherichia coli*.

This patient had dietary deficiency, chronic liver disease, and acute liver failure. Chart 10 illustrates the course of the prothrombin levels and shows the lack of response to vitamin  $K$  therapy.

L. F. D., No. PHB H 356922, a 40 year old man, entered the hospital because of epigastric pain and

hematemesis of 24 hours' duration. For 10 years he had been a heavy drinker. During the 4 days before entry he drank steadily and ate little food. He had vomited repeatedly during the 24 hours before entry.

Examination revealed an obese white man retching and hiccupping. The sclerae were icteric and injected. The tongue was dry and coated. The liver extended from the fourth interspace to a level 3 finger-breadths below the costal margin in the mid-clavicular line. The abdomen was large with tenderness in the right upper quadrant. Laboratory data were as follows: white blood cells, 15,000 with 82 per cent neutrophils, urine showed albumin and bile, urobilinogen, strongly positive, the stool was brown with bile, guaiac, positive icterus index, 31, bromsulphalein test showed 30 per cent retention after 10 minutes.

For 2 days the patient subsisted on parenteral fluid only. On the third hospital day he had numer-

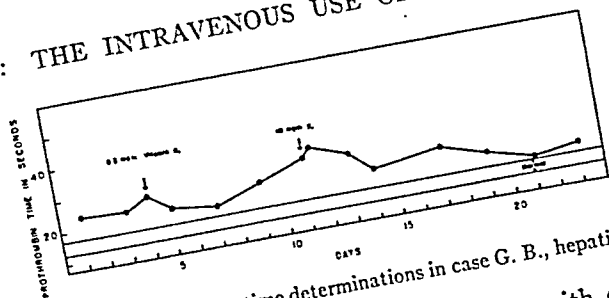


Chart 13. Prothrombin time determinations in case G. B., hepatitis.

ous ecchymoses and some bleeding about the needle puncture wounds. The prothrombin time was 33 seconds. He was given 10 milligrams of vitamin K<sub>1</sub> intravenously. No bleeding was noted thereafter, and the ecchymoses cleared. The patient improved markedly and was discharged well on the fourteenth hospital day.

This chronic alcoholic had an acute hepatitis from which he recovered. The interpretation of the response of prothrombin level to vitamin K therapy must therefore be guarded. The vitamin was given at a time when the patient was acutely ill and was taking nothing by mouth. Chart 11 illustrates the fall in prothrombin time and suggests a definite therapeutic effect. This response was not as rapid as had been noted in cases of obstructive jaundice and biliary fistula.

S. M., No. B.I.H. 50239, a 53 year old man, entered because of progressive dyspnea, ascites, and edema of 6 months' duration. Examination disclosed pallor, slight icterus, massive ascites, and pitting edema from the waist down. The laboratory data were as follows: red blood cells, 3,400,000; hemoglobin, 70 per cent; white blood cells, 4,600; normal differential; most urine specimens contained albumin, bile, and white blood cells; urinary urobilinogen 1:320; stools brown, guaiac, negative; non-protein nitrogen, 39; icterus index, 23; urea nitrogen 9.5; total protein, 4.8; albumin, 1.9; globulin 2.9.

Abdominal paracentesis yielded 2200 cubic centimeters of fluid following which the dyspnea was relieved. Peritoneoscopy disclosed a small, pale, granular liver suggesting portal cirrhosis, and an enlarged spleen. The patient was treated by diuretics, hypertonic glucose intravenously, a high protein diet supplemented by transfusions and liver extract intramuscularly. He lost much of his accumulated fluid but there was no significant improvement in the anemia, the icterus, or the blood protein level. After a month in the hospital the patient suddenly lost consciousness. It was felt that a cerebral vascular accident had occurred. He remained in coma for 48 hours and died.

The prothrombin times in the last 2 weeks of life varied between 20 and 28 seconds, rising terminally. During this period vitamin K was given.

This patient with clinical cirrhosis of the liver had a low-grade prothrombin deficiency. The prothrombin time was not altered by repeated large doses of the water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone. To determine whether the lack of response resulted from failure of conversion of the ester to the quinone, perhaps because of inadequate liver function, a large dose of the uncombined naphthoquinone was given intravenously. Again, however, no favorable response was obtained. Vitamin K<sub>1</sub> was given just a few hours before the patient's death so that any effect it might have had could not be determined. The prothrombin levels are recorded in Chart 12.

G. B., No. B.I.H. 55553, a 29 year old white female, entered complaining of swelling of the abdomen and legs of 5 days' duration. She had been jaundiced for a week after scarlet fever at the age of twelve. Mild jaundice had been noted 4 years before admission. Four weeks before admission the present illness started with an acute respiratory infection followed by persistent malaise, weakness, and mild icterus, and then by swelling of the abdomen and enlarged eyes. Examination disclosed jaundice, enlarged velvety of the breasts, marked ascites, dilated liver and spleen (palpable after paracentesis), dilated venules over abdomen, edema of lower extremities and sacrum. Laboratory data included: bile in urine; urinary urobilinogen 1:640; white blood cells, 3000; neutrophils, 84; lymphocytes, 16; icterus index, 20; cholesterol, 152; cholesterol ester, 68; total protein, 5.3; albumin, 1.9; globulin, 3.4; urea nitrogen, 5.8; hippuric acid excretion, 0.58 gram in 4 hours. The bleeding time, 2½ minutes, the clotting time, 3½ minutes, and the prothrombin time, 25 seconds.

Treatment consisted of limitation of fluid intake, high carbohydrate, high protein, low-fat diet, concentrated glucose intravenously, oral and parenteral vitamins A, B group, C, and D concentrates, ammonium chloride orally and mercupurin intravenously, and abdominal paracenteses. During the part of her hospital stay in which she received intravenous vitamin K therapy there was no evidence of improvement either clinically or by laboratory tests.

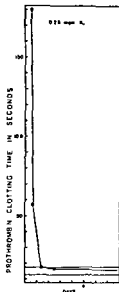


Chart 14

Chart 14 Prothrombin time determinations in case P A R, newborn infant

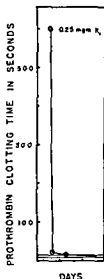


Chart 15

Chart 15 Prothrombin time determinations in case A B, newborn infant

During this period she suffered menorrhagia and intermittent bleeding from the gums.

This patient whose clinical picture suggested chronic hepatitis with acute exacerbation was treated with 0.3 milligram and again with 10 milligrams of vitamin K<sub>1</sub> intravenously. No significant effect was noted. The prothrombin time determinations are shown in Chart 13.

In agreement with Butt and co-workers, and Warner, it was found that the prothrombin deficiency of severe primary liver disease responded poorly to vitamin K therapy. In only one case (L. F. D) was a significant effect suggested. This was noted in the acute phase of a hepatitis from which the patient recovered.

In the few cases of liver disease studied the prothrombin deficiency was for the most part of low grade, no prothrombin time above 40 seconds being encountered except terminally.

#### Newborn Infants

The results in newborn infants are presented in the following cases

P. A. R., No. C. H. 240549<sup>1</sup>, a female baby, entered 3 days after a breech delivery. The patient was said to have been cyanotic and limp during the first 3 hours of life. This was followed by muscular twitching and the passage of dark, reddish stools. Physical examination revealed a well developed infant with mild convulsive twitchings of the left extremities, slightly irregular respirations, and rotary nystagmus. The patient was hypotonic and unresponsive. There was a cephalohematoma over the right and left parietal bones. The disc of the left eye was somewhat indistinct, extremities were cold and cyanotic, right arm was limp, and the left arm hypertonic. The prothrombin time on admission was 3 minutes, and the patient was given 0.25 milligram of vitamin K<sub>1</sub> intravenously.

Cerebrospinal fluid was bloody and xanthochromic during the first week, but this gradually cleared. Stools were bloody for a few days but then became guaiac negative. Small ecchymotic spots over the scalp and lower extremities disappeared, and the infant showed marked improvement, but it was felt at the time of discharge that she still had obvious cerebral deficiency.

This newborn baby with hemorrhagic tendency and prothrombin deficiency received vitamin K therapy after intracranial hemorrhage had occurred. The prothrombin time dropped from 180 seconds to normal within 12 hours. The prothrombin times are recorded in Chart 14.

A. B., S. Hosp.<sup>2</sup>, a newborn male, was delivered without forceps after labor of 21 hours. Baby was first seen 36 hours after delivery because he was spitting up blood and bleeding from the umbilicus.

Examination disclosed bright blood oozing from the hard palate and fresh bleeding from the umbilicus. Red blood cells, 4,900,000, white blood cells, 16,000, hemoglobin, 104 per cent. Bleeding time was less than 3 minutes, and clotting time less than 5 minutes. The prothrombin time was over 10 minutes.

On the second day of life, the baby was given 0.25 milligram of vitamin K<sub>1</sub>. No transfusion was given and the bleeding stopped within an hour. The baby was discharged in good health.

This newborn baby with hemorrhagic tendency and prothrombin deficiency stopped bleeding within 1 hour after vitamin K<sub>1</sub> was given. The prothrombin time dropped from 600 seconds to 21 seconds within 4 hours. The prothrombin time determinations are recorded in Chart 15. In this patient a hemorrhagic

<sup>1</sup>Acknowledgment is made to the Children's Hospital for permission to study this case.

<sup>2</sup>Acknowledgment is made to the Salem Hospital for permission to study this patient.

tendency was associated with a prothrombin deficiency despite normal clotting and bleeding times.

B. H., No. C.H. 244563<sup>1</sup>, a 3 day old male baby, entered the hospital because of persistent vomiting since birth. The delivery was at term after a normal pregnancy. Examination of the baby at birth was not unusual; birth weight 7 pounds, 8 ounces. The baby retained nothing taken by mouth from birth. He vomited repeatedly, the vomitus containing bile. Both vomitus and stool were noted to contain blood the day before admission. Saline by clysis and an unknown amount of blood intramuscularly were given 6 hours before admission. On admission, the baby was noted to be dehydrated, the umbilicus and penis were oozing blood, and a needle puncture wound in the heel made 10 hours earlier continued to bleed. The laboratory data included: red blood cells, 5,220,000; hemoglobin, 118 percent; white blood cells, 11,450; vomitus and stool guaiac, positive; blood culture and serology, negative; capillary clotting time 7 minutes; prothrombin time, 115 seconds.

The baby was given 0.25 milligram of vitamin K<sub>1</sub> intravenously. Within 3 hours the bleeding from the umbilicus, the penis, and the needle puncture wound had stopped, and the capillary clotting time was 3 minutes. The prothrombin time 12 hours after injection of vitamin K<sub>1</sub> was 18.5 seconds. Difficulty in obtaining venous blood prevented further prothrombin readings, but repeated clotting times remained at 3 minutes.

The vomiting continued. Vomitus and stools examined 3 days after the administration of the vitamin were guaiac negative. A diagnosis of duodenal obstruction was made, and laparotomy was done on the eighth day of life, the fifth day after therapy of the hemorrhagic disease. No further vitamin K and no blood were given before operation. At operation, congenital volvulus of the intestine with duodenal obstruction was found and corrected. There was no unusual bleeding during the procedure. The convalescence was uneventful. Transfusions of 65 and 75 cubic centimeters of whole blood were given on each of the first two postoperative days. The baby was able to take food and had gained weight.

Because of the persistent vomiting, the active hemorrhagic tendency could be treated effectively only by the parenteral route in this case. The rapid restoration of normal blood coagulability permitted surgical correction of the duodenal obstruction. A rapid and maintained response to a single dose of intravenously administered vitamin K<sub>1</sub> was noted. It is interesting to speculate on the rôle played

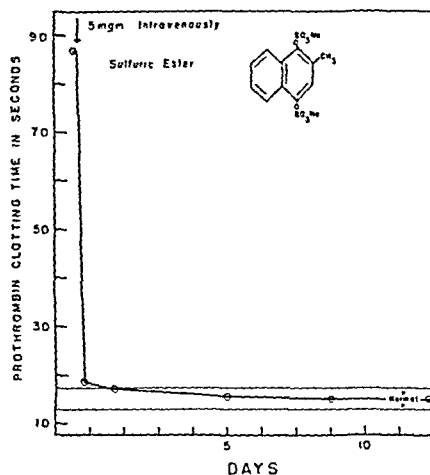


Chart 16. Prothrombin time determinations in case E. S., newborn infant.

by the congenital duodenal obstruction in the development of hemorrhagic disease in this instance.

D. S., No. B.L.I.H. 29163<sup>2</sup>, a male baby, was delivered with low forceps. The patient did not breathe until lobeline was administered. Two days after delivery, bleeding from the forceps scar and bilateral tense cephalohematomas were noted. The baby did not nurse well, had a high-pitched cry, and tense fontanelle. Subdural taps revealed no blood. The prothrombin time was 62 seconds. Five milligrams of the sodium salt of the sulfuric ester of 2-methyl-1,4-naphthohydroquinone was given intravenously. Bleeding stopped within an hour. The baby recovered.

This newborn baby with hemorrhagic tendency and prothrombin deficiency stopped bleeding within one hour after the water soluble vitamin K preparation was administered intravenously. The prothrombin time dropped from 62 seconds to 24.5 seconds within 3 hours and to 16 seconds within the next 24 hours.

E. S., No. B.L.I.H. 28520<sup>2</sup>, a female baby, following a normal, multiparous delivery vomited blood on the second and again in the evening of the third postpartum day. Physical examination was negative. The prothrombin time was 87 seconds. The patient was given 5 milligrams of the sodium salt of the sulfuric ester of 2-methyl-1,4-naphthohydroquinone intravenously. There was no further abnormal bleeding.

<sup>1</sup>Acknowledgment is made to the Children's Hospital for permission to study this case.

<sup>2</sup>Acknowledgment is made to the Boston Lying-In Hospital for permission to study this case.



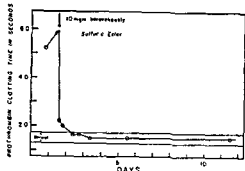


Chart 17 Prothrombin time determinations in case R. MacQ, newborn infant

This newborn baby with hematemesis and prothrombin deficiency was given 5 milligrams of the water soluble vitamin K preparation. The prothrombin time dropped from 87 seconds to 18 seconds within 4 hours and remained normal thereafter. The prothrombin determinations are shown in Chart 16.

R. MacQ, No. C.H. 23817<sup>81</sup>, a male baby, was admitted at the age of one day with history of vomiting blood 14 hours after delivery followed by the passage of grossly bloody stools. At birth the patient had received 30 cubic centimeters of blood intramuscularly. Examination on admission revealed a left cephalohematoma and brisk bleeding from the rectum. Laboratory data included: red blood cells, 2,360,000; hemoglobin, 36 per cent, bleeding time, 15 minutes; capillary clotting time, less than 3 minutes, prothrombin time, 52.5 seconds.

Shortly after admission 75 cubic centimeters of blood were injected intramuscularly. Fifteen hours later the prothrombin time was 58.5 seconds and the baby was given 10 milligrams of the sodium salt of the sulfuric ester of 2-methyl-1, 4-naphthohydroquinone. The abnormal bleeding stopped promptly.

This baby with hemorrhagic disease observed within 14 hours after delivery despite intramuscular blood given at birth, received more adult blood intramuscularly which again failed to lower the prothrombin time or to stop the bleeding. The water soluble vitamin K preparation given intravenously resulted in a drop in prothrombin time to 22 seconds within 4 hours. The prothrombin time determinations are recorded in Chart 17. The gross clotting time in this case was not elevated although the prothrombin clotting time was

markedly prolonged and the clinical bleeding was profuse.

Waddell and Guerry; Quick and Grossman (14); Rhoads and Fliegelman; Shettles, Hellman, and Delfs; and Nygaard have reported the successful oral treatment of hemorrhagic disease of the newborn with extracts containing vitamin K<sub>1</sub>, or with 2-methyl-1, 4-naphthoquinone. The cases treated with synthetic vitamin K<sub>1</sub> intravenously showed a rapid response to a single small dose (0.25 milligram in 25 cubic centimeters of solution). In no case was a second dose necessary.

The cases<sup>2</sup> treated with the sodium salt of the sulfuric ester of 2-methyl-1, 4-naphthohydroquinone intravenously responded in the same way—5 milligrams of the ester and 5 milligrams of sodium bicarbonate in 5 cubic centimeters of water. Because of the solubility of the sulfuric ester smaller volumes may be used. Alkaline solutions of the sulfuric ester are not light sensitive.

#### EVALUATION OF STUDY

A group of substances capable of correcting the low blood prothrombin levels of certain clinical and experimental conditions, is described as having "vitamin K" activity. These substances, as found in nature, are all quinones, or are readily transformed into quinones. The quinones are almost completely insoluble in water but dissolve in fat solvents. Vitamin K<sub>1</sub>, the original principle as found in alfalfa, has been isolated, its structural formula has been elucidated as 2-methyl-3-phytyl-1, 4-naphthoquinone and it has been synthesized (5, 7). A large group of related compounds has been synthesized and found to have vitamin K activity by chick assay (9). Many of these substances have been used clinically (Fig. 1).

The lack of solubility in water of naturally occurring vitamin K is responsible both for the development of a large part of clinical vitamin K deficiency, and for much of the difficulty of therapy. In obstructive jaundice and in biliary fistula the absence of bile salts

<sup>1</sup>Acknowledgment is made to the Children's Hospital for permission to study this case.

<sup>2</sup>Since these data were compiled a water soluble hyalofite derivative of 2-methyl-1, 4-naphthoquinone (Abbott's hyalofite) has been used in hemorrhagic disease of the newborn with similar results—dose: molecular equivalent of 5 milligrams of the naphthoquinone.

in the intestinal tract reduces the absorption of all fat soluble substances. This situation creates the largest group of vitamin K deficiencies. Disease of the gastro-intestinal tract severe enough to interfere with general absorption and nutrition, despite the normal flow of bile, may result in inadequate absorption of vitamin K as shown by altered blood prothrombin levels. It has been pointed out that the liver plays an important rôle in the maintenance of the blood prothrombin. Removal or poisoning of the liver in experimental animals results in a fall in blood prothrombin which cannot be corrected by vitamin K therapy. In clinical liver failure hypoprothrombinemia frequently develops.<sup>1</sup> Investigators have found this condition refractory to vitamin K therapy (4, 23). More recently prothrombin deficiency has been noted in the blood of many newborn infants. The diminution of blood prothrombin is marked in "hemorrhagic disease" of infancy, and readily responds to vitamin K administration.

The earliest efforts at vitamin K therapy made use of crude extracts of varying potency. The isolated principles were used as soon as they became available. Because of their insolubility in water, therapy was largely confined to oral administration, with the addition of bile salts when these were absent from the intestine. The need for an effective parenteral method of therapy became apparent. Nausea, vomiting, intestinal obstruction, or other types of interference with intestinal absorption frequently prevented restoration of normal blood coagulability, often in the patients most in need of effective treatment. Both subcutaneous and intramuscular injection of substances with vitamin K activity proved to have too slow an effect in the presence of bleeding and in preparation for surgery. A method of preparing pure vitamin K<sub>1</sub> in colloidal suspension for intravenous administration has been described (10). This mode of therapy has been found to be rapidly effective, the uncertainties of intestinal absorption are eliminated, and the action of the drug has been noted to be prolonged. 2-Methyl-1, 4-naphthoquinone was effective when used in

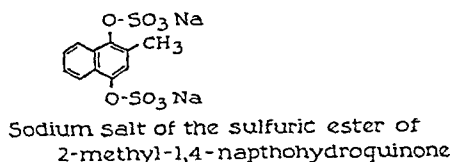
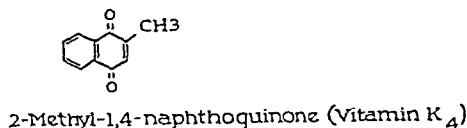
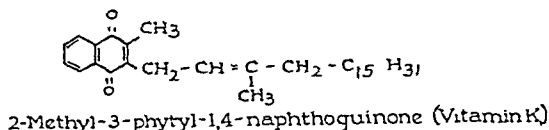


Fig. 1. Formulas for vitamins K<sub>1</sub>, K<sub>4</sub>, and sodium salt of the sulfuric ester of reduced vitamin K<sub>4</sub>.

the same way. On the basis of minimal effective dosages shown by chick assay, 2-methyl-1, 4-naphthoquinone is fully as active as vitamin K<sub>1</sub> (1). However, clinical trials suggest that a single dose of vitamin K<sub>1</sub> has a longer effect than that of an equivalent dose of 2-methyl-1, 4-naphthoquinone.

Several points of physiological interest are brought out by intravenous vitamin K<sub>1</sub> therapy. The blood prothrombin level is very rapidly restored following the correction of vitamin K deficiency. This may occur even in a moribund patient. The prolonged effect of large—10 milligram—doses as compared with that of small—0.5 milligram—doses, suggests the possibility of storage within the body of vitamin K<sub>1</sub>, or of some derivative of the quinone. The physical properties of vitamin K<sub>1</sub> suggest that it may not be rapidly excreted. Studies of the complete metabolism of the quinone, however, have not been reported. The intravenous route obviates the changes in chemical form which may occur within the intestinal tract and offers a method for the comparison of the activity of various anti-hemorrhagic substances. Such comparisons must be made with caution in view of the necessarily uncontrolled nature of the clinical experiments.

The search for parenterally effective vitamin K preparations has led to the synthesis of water soluble compounds. The use of these

<sup>1</sup>A review of the evidence for the rôle of the liver in the development of hypoprothrombinemia may be found in a summary by Brinkhous.

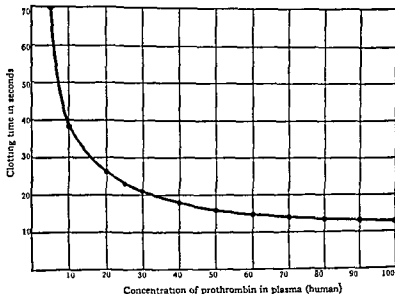


Fig 2 Determination of prothrombin in human plasma. The relation of the clotting time of recalcified plasma, containing an excess of thromboplastin, to the concentration of prothrombin (Courtesy A J Quick, *J. Am M Ass.*, March 14, 1938)

substances eliminates the need for the large volume of fluid used in suspending the quinone. A report on the intravenous use of a bisulfite derivative of 2-methyl-1, 4-naphthoquinone was recently published by Kark and Souter. They found that 48 hours were required for the return to a normal prothrombin time and noted that the effect lasted less than 24 hours. Slow conversion to an active form together with rapid excretion of a water soluble substance may account for these findings. The authors reported no better effect with larger doses. Our experience with a sulfuric ester of 2-methyl-1, 4-naphthohydroquinone disclosed a similar slow and short effect which was not improved by giving 20 milligrams instead of 10 milligrams. The water soluble compounds thus differ markedly from the quinones, in that increasing the dose of the quinones does intensify and prolong their effect.

Reference to Quick's demonstration of the relationship of prothrombin time to concentration of prothrombin (13) demonstrates that the formation of comparatively small amounts of prothrombin will result in a rapid drop from a high to a moderate prothrombin time (Fig. 2), but that larger amounts are required to

reduce the prothrombin time to normal. A prothrombin time within normal limits may represent large variations in prothrombin concentration. The prothrombin curves published by Kark and Souter flatten distinctly before the normal level is reached, and a similar effect was noted by us in studying the action of the sulfuric ester and of small doses of the quinones.

Because all other clinical instances of prothrombin deficiency responded to vitamin K administration, the effect of vitamin K on the hypoprothrombinemia of liver disease was studied. The investigation seemed of interest, although we had not encountered a patient with liver disease whose prothrombin deficiency led to abnormal bleeding of clinical significance. Although prothrombin deficiency in liver failure is probably unrelated to vitamin K deficiency, it was thought that an excess of vitamin K might possibly increase prothrombin production. The recognition of small responses to therapy was difficult because the blood prothrombin levels in patients with liver disease were observed to vary spontaneously. In general, the prothrombin deficiency of liver failure was not improved by

vitamin K. In one instance of liver failure from which the patient recovered, a return to a normal prothrombin level followed the administration of vitamin K intravenously. This response was very different from the characteristic reaction to the vitamin in other prothrombin deficiencies in that the return to normal required 72 hours (see Chart 11).

#### CONCLUSIONS

1. Vitamin K<sub>1</sub>—2-methyl-3-phytyl-1, 4-naphthoquinone—can be dispersed in glucose solution and in this form it can be safely administered intravenously.

2. A single 10 milligram dose of vitamin K<sub>1</sub> given intravenously in cases of obstructive jaundice and biliary fistula produced a more rapid and prolonged effect than any other substance so far reported.

3. Single doses of 0.25 milligram of vitamin K<sub>1</sub> or of 5 milligrams of the sodium salt of the sulfuric ester of 2-methyl-1, 4-naphthohydroquinone resulted in rapid cures of hemorrhagic disease of the newborn.

4. The prothrombin deficiency of liver failure did not respond to vitamin K except in one instance in which clinical recovery occurred.

5. 2-Methyl-1, 4-naphthoquinone has been administered intravenously as a colloidal suspension and has been found to be effective by this route.

6. A water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone was capable in 10 to 20 milligram doses of causing distinct drops in prothrombin time, but in the degree, rapid-

ity and duration of its effects, it was found to be inferior to the quinones.

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## HIP FRACTURES

### Treatment by the Multiple Kirschner Wire Method

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THE multiplicity of methods used in treating hip fractures is sufficient proof that no perfect method has been evolved. The percentage of results which might be classified as excellent, or even satisfactory, is still too low, though unquestionably far greater than was the case 10, or even 5, years ago. The reasons for being unable to evolve a universally successful method of treatment are perhaps insurmountable. Probably chief among these is the fact that this fracture is common in the aged and relatively rare in youth. A mechanical reason is the difficulty of proper reduction due to the freely movable billiard ball like femoral head unattached or held by any strong ligament, with the added possibility of interposition of torn capsule. A still further reason, physiological in nature, and probably more important in the case of the femoral neck as opposed to intertrochanteric fractures, is the fact that the main blood supply of the femoral head is derived from capsular arteries which enter the base of the neck extending into and anastomosing in the head. When this blood supply is broken off, unless restored by good and close approximation of the fragments, death and aseptic necrosis of the head will surely result. It has been conceded by almost all orthopedists that the minute blood supply through the ligamentum teres is not sufficient to nourish the head; so in order to prevent death of the fractured head and nonunion, it is absolutely essential to procure early reduction and firm fixation of the fragments so that the disrupted circulatory lines of communication will be quickly re-established. This aseptic necrosis of the head has been recognized for a great many years, being first described by Sir Astley Cooper over a hundred years ago, and as late as 1896 Kocher thought that death and aseptic necrosis of the head took place in *all* femoral neck fractures.

A brief review of the evolution of the treatment of hip fractures recalls that the first great advance was introduced by Whitman in 1912 and consisted of his classical reduction by abduction, flexion, extension, and internal rotation followed by fixation in a body plaster spica. With the Whitman technique, bony union was not claimed

for more than 40 to 60 per cent of cases. Its most serious defect was the prolonged immobilization leading to pulmonary complications in the aged. This fact was a stimulus to orthopedists in the development of methods which would not only give firm fixation but also allow early mobilization of the patient. To fill both of these requirements some form of mechanical fixation was obviously necessary. However, until the work of Smith-Petersen, first published in 1931, mechanical fixation had been largely limited to the use of the round nail or bone peg driven through the trochanter into the head. In the case of the former, fixation was not complete due to rotation of the head on the nail which served as an axis. In the case of the latter, fixation was very unstable due to weakness and frequent breakage of the bone peg. Smith-Petersen overcame this disadvantage of the nail by developing a flanged nail which definitely prevented rotation of the fragments. His nail was later greatly improved by canalization (Johansson), which allowed more accurate insertion of the nail over a Kirschner wire. Since his pioneer work, a number of mechanical devices have been developed which have certain advantages over the nail in that they not only fix but impact and hold the fragments in impaction. Examples are the Henderson lag screw, the Morrison lock bolt, the Moreira stud bolt screw, the Martin multiple screws, and many others. All of these methods of mechanical fixation require a rather elaborate armanentarium to be carried out properly, not to speak of considerable practical experience not available to all surgeons required to treat hip fractures. In the absence of these two requirements, depressing accidents occur, the most common of which is splitting of the trochanter major, neck, or the femoral head itself (Fig. 1). Suffice it to say, hip fractures are one condition in which accidents are an ill afforded luxury, permanent crippling of the patient being the usual unfortunate result. When this happens, just as usual, little can be done to improve the patient's condition.

It is the purpose of this paper to present our experience with as near a foolproof mechanical method of fixation in hip fractures as we believe has yet been devised. The multiple Kirschner

## CHESTER: HIP FRACTURES

wire method apparently was first used extensively in this country by Dyas and Aries, of Chicago, who published their results in the October, 1936, issue of *SURGERY, GYNECOLOGY AND OBSTETRICS*. This method had been previously used, though not so successfully, by orthopedic surgeons in Norway and other countries. Since publication of the Dyas and Aries article, there have been several other articles published by men who tried the method with less success; in fact, most of the publications since were for the purpose of condemning the method. However, it would appear that most of the reasons given for this condemnation were the result of carelessness in the hands of the orthopedists who had used it rather than of any inherent fault in the method itself. One criticism is that there is danger of drilling the Kirschner wire through the acetabulum into the pelvis and puncturing some of the large vessels. In careless hands this has actually happened but is inexcusable. Others have stated that the wires tended to migrate, either burying themselves in the bone so as to make removal difficult (Fig. 6 c) or even going so far as to lose themselves in the soft tissue or pelvis. The first argument might as reasonably be used against surgical opening of the abdomen or any other surgical procedure in which accidents caused by the operator's carelessness might occur. The second accident noted can easily be prevented as will be shown.

Advocates of the flanged nail have claimed more speed for their method. Even if true, we do not consider speed to be a great necessity when the



Fig. 1. Female, aged 70 years. Accident resulting from the insertion of a Smith-Petersen nail. Roentgenogram made 3 years after original nailing. Patient was brought to my attention by medical service to which she was admitted for generalized arteriosclerosis and cardiac disease. She had been bed-ridden since operation. A, Sclerotic blood vessel; B, apparently portion of greater trochanter; C, partially absorbed femoral head; D, cap of Smith-Petersen nail.

technique is practically shockless. However, when the nail is threaded over a Kirschner wire, we have found it usually necessary to insert several wires before the accurate placement or centering necessary for use of the nail is secured. When this

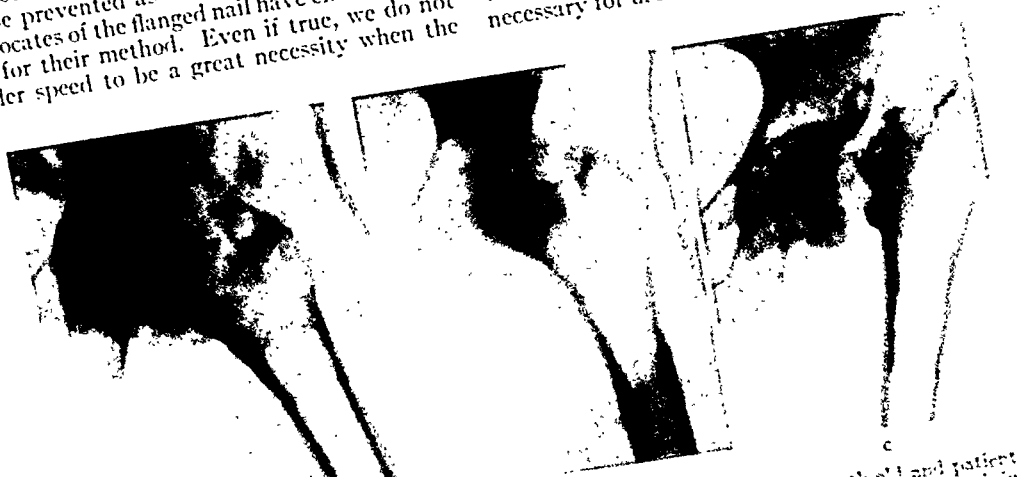


Fig. 2. Anteroposterior, lateral, and patient

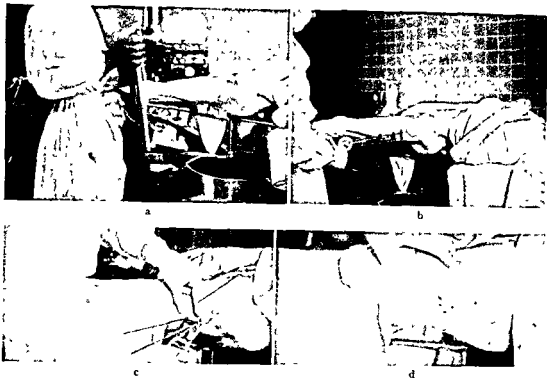


Fig 3 Case 1. Male, aged 54 years. a, Fracture has been reduced by manipulation under local anesthesia and is held fixed by Scantle-Balfour table. Photograph shows preparation for check of position by lateral roentgenogram. Curved cassette with portable machine placed laterally is better if available. Note guide wire A extending from greater trochanter and bisecting Poupert's ligament. b, Insertion of first Kirschner wire. Note circle of skin anesthesia about area through which wires will be passed. Known position of guide wire with relation to femoral neck

assists in determining direction of Kirschner wire. c, Kirschner wires being clipped after checking proper depth and position by x ray film. Wires should be bent at bone surface before clipping to prevent occasional complication of migration (Fig 4e). Skin about wire depressed before cutting of wire ends. d, Operative site immediately after wires have been clipped below skin level and skin allowed to cover all wire ends. Operation has been completed and no further fixation of fracture is required in most instances.

is necessary the Kirschner wire method might require less time than the nailing operation.

We first began using this method of treatment in hip fractures in December, 1936, after publication of the work of Dyas and Aries. With minor changes in technique it has since become routine with us whenever applicable. When properly applied the technique is one which is almost entirely free of shock to the patient, requires no skin incision, and yet fulfills the two criteria of firm fixation of the fracture with early mobilization of the patient. It consists essentially of the fixation of the fragments by the insertion of multiple Kirschner wires so placed as to utilize the crossed nail locking principle well known to carpenters. In other words, the wires are placed at widely varied angles which locks the head in place in a manner impossible for wires placed in parallel

planes. We first attempt to secure accurate reduction of the fracture. This is done manually after the patient is placed on the fracture table and the well leg is fixed in the foot piece so as to anchor the pelvis firmly. We have found local anesthesia perfectly satisfactory for accomplishing reduction.

Preoperative preparation is important. Our custom is to administer one of the barbiturates the night before the operation and again 30 minutes before taking the patient to the fracture room. Morphine from  $\frac{1}{6}$  to  $\frac{1}{4}$  grain and scopolamine  $\frac{1}{200}$  grain are given at the same time. With this preparation we have found the patient to sleep intermittently throughout the operation, and shock incident to the trauma involved is minimal or absent. In the administration of the local anesthetic we attempt to locate the joint

## CHESTER: HIP FRACTURES

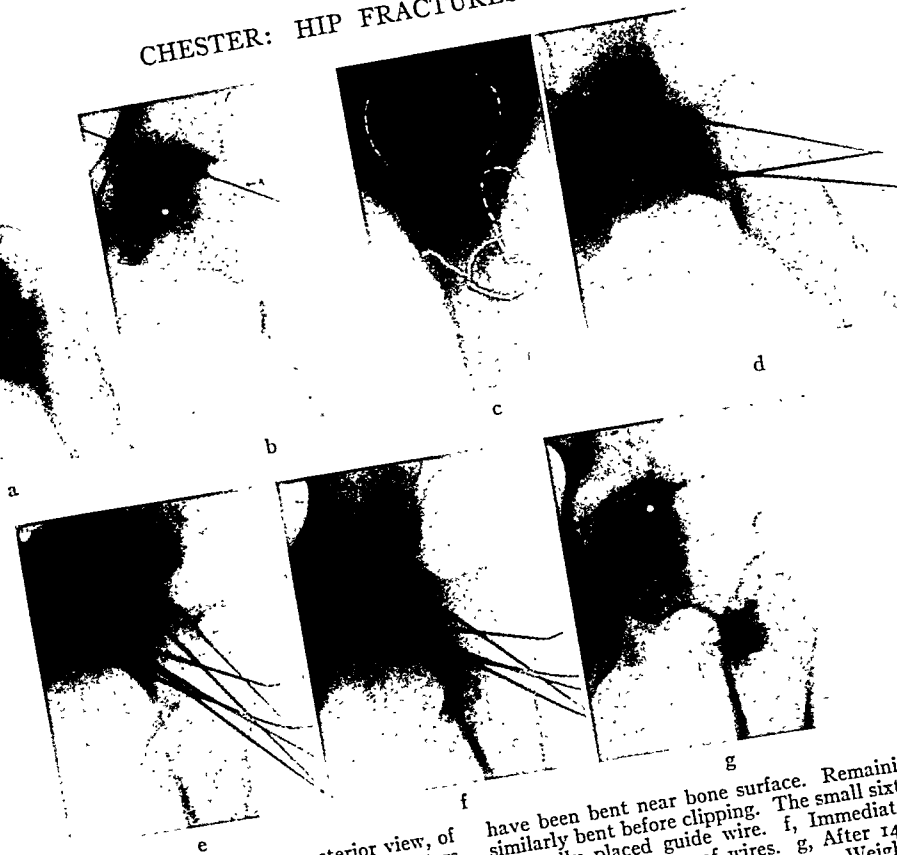


Fig. 4. Case 1. a, X-ray film, anteroposterior view, of fracture through base of femoral neck and trochanters before reduction. b, Same patient after reduction showing external guide wire A following fairly accurately the normal line of the femoral neck. This x-ray film corresponds to photograph, Figure 3a. c, Lateral view proving accurate reduction. d, After insertion of 2 Kirschner wires purposely not far enough. e, After insertion of all 5 wires. Two wires

have been bent near bone surface. Remaining 3 will be similarly bent before clipping. The small sixth wire is the externally placed guide wire. f, Immediately following bending and clipping of wires. g, After 14 months and immediately after removal of wires. Weight bearing for past 9 months. Firm bony union is present and the removal of the wires could have been done with safety several months earlier.

capsule by introduction of a long needle until bloody synovial fluid can be aspirated and then we inject 20 cubic centimeters of 2 per cent procaine directly into the joint. If difficulty is met in definitely locating the joint capsule, the anesthetic may be merely injected about the joint, slightly more being required in this event. Reduction is accomplished manually by a manipulative method which combines portions of the technique of both Ledvetter and Whitman, varied, of course, with the different types of fractures. Essentially, it consists of flexion of the joint to about 35 degrees, external rotation, abduction, traction, followed by internal rotation and extension accomplished in one movement. We sometimes find it necessary to vary this by having an assistant apply lateral traction to the hip by pulling laterally on the upper thigh while manipulation is being carried out. After comple-

tion of the manipulation, the involved extremity is fixed in abduction, extension, and internal rotation by fastening the foot to the footpiece of the fracture table. Before reduction is checked by roentgenography, a Kirschner wire is fixed to the skin anteriorly bisecting Poupert's ligament and pointing outward and downward to the greater trochanter with the shaft of the greater wire so placed usually follows fairly accurately the normal line of the femoral neck. Roentgenograms, both anteroposterior and lateral, are now made with the portable machine to check reduction. If satisfactory, we are ready to proceed with the insertion of the Kirschner wire drills. The guide wire previously noted is now indispensable in indicating the direction for inserting the wires in the horizontal plane. For the vertical plane, fixation of the extremity at 25 degrees



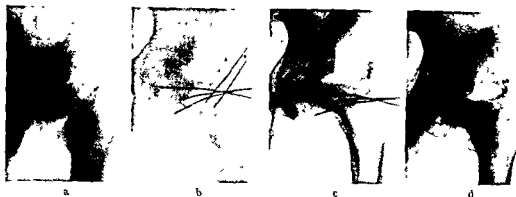


Fig 5 Case 2 Male, aged 19 years a, Roentgenogram of fracture of base of femoral neck showing marked rotation and displacement b, This patient, a C. C. C. enrollee, was admitted 2 months after injury and, because of fixation, accurate manual reduction was not possible. Open reduction using the Olier approach was done. Fragments freshened, approximated, and fixed by 3 Kirschner wires. Trochanter major A, which was removed with muscle attachments for exposure, reattached with 2 crossed Kirschner wires B. Traction was applied to this patient for 6

weeks. On removal angulation at fracture site promptly took place with bending of wires. Use of 2 more wires originally would undoubtedly have prevented this. c, X ray film taken 8 months after operation showing firm bony union. Wires holding trochanter removed after 10 weeks. Wires through neck allowed to remain for 12 months. d, Immediately after removal of wires. Three-quarters of an inch shortening due to varus position of neck caused by original angulation and bending of wires at site of fracture. Function normal.

internal rotation results in an almost flat plane of the neck parallel to the floor. For anesthesia at this point, we find that it is sufficient to anesthetize a fairly wide circle of skin extending from approximately  $\frac{1}{2}$  inch below the trochanter major to its upper border. This leaves the area directly over the point of insertion of the wires uninfiltreated, so that one is allowed to palpate the bone with relative ease. Two 16-gauge Kirschner wires are now passed through the lower portion of the trochanter, or shaft just below the trochanter, into the neck and head of the femur, the guide wire being used to determine direction (Fig 3b). These 2 wires are purposely *not* inserted far

enough so as to avoid any danger of inserting them too far (Fig. 4d). Another anteroposterior and lateral check at this point enables us to determine by measurement on the roentgenogram, the exact distance necessary further to insert the 2 wires. Accuracy is obtained by nicking the wires at this exact distance from the skin and then continuing their insertion until this nick reaches the skin. We now have 2 wires properly placed and their direction accurately checked on the roentgenogram. By the use of these as guides and direction finders, the remaining 3 wires can be easily inserted to the proper depth and in the proper direction. After all 5 wires are in place, it is

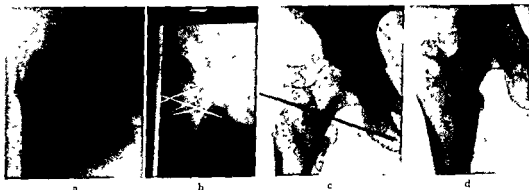


Fig 6 Case 3 Female, aged 74 years a, Comminuted, intertrochanteric fracture, right hip b, After fair reduction and fixation by 4 Kirschner wires. This was an early case and wires were not bent at bone surface, resulting in migra

tion of upper wire as shown in Figure 6c. c, After removal of 3 wires. The fourth wire has migrated to trochanteric surface and required an incision for removal. d, X-ray film after 1 year showing solid bony union.

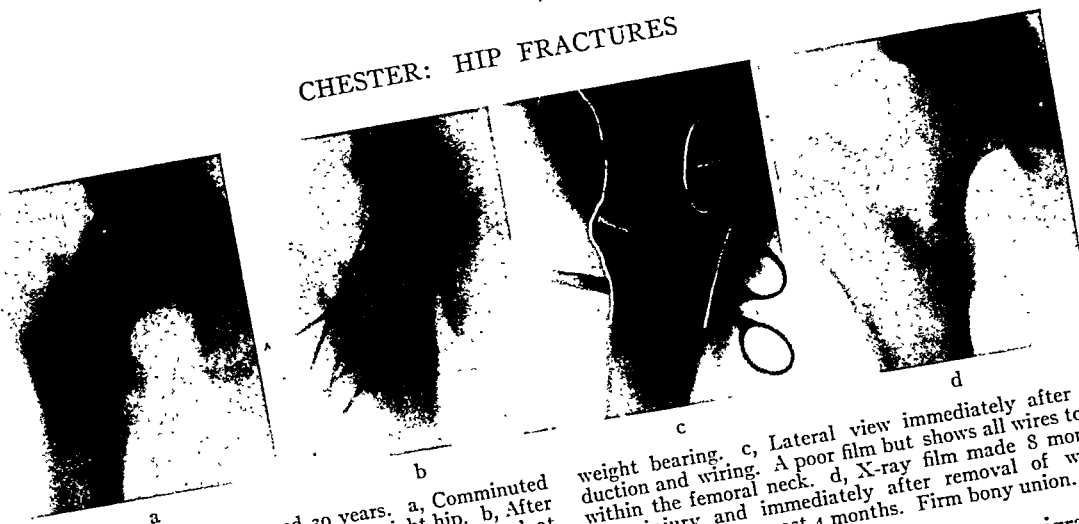


Fig. 7. Case 4. Male, aged 39 years. a, Comminuted fracture through base of femoral neck, right hip. b, After reduction and fixation by 5 Kirschner wires crossed at widely divergent angles. Upper wire A inserted a fraction too far, but caused no symptoms even after beginning

weight bearing. c, Lateral view immediately after reduction and wiring. A poor film but shows all wires to be within the femoral neck. d, X-ray film made 8 months after injury and immediately after removal of wires. Weight bearing for past 4 months. Firm bony union.

our practice to take a third series of roentgenograms to check the position of the wires. If all is satisfactory and no further adjustments are necessary, each wire is grasped in turn and sharply angled at its point of exit from the femur, after which, the skin is pressed down approximately  $\frac{3}{8}$  inch at which point the wires are cut, and the skin allowed to come out over the ends of the wires leaving a closed operative field (Fig. 3, c and d). Bending the wires at the bone is im-

portant, as it will definitely inhibit the migration or slipping of the wires further into the bone, a point of objection to this method raised by some orthopedists as we have already noted.

The operation is now complete, and it is optional with the surgeon whether or not he wishes to apply skin traction at the extremity for a few days until muscle spasm, normally present in any fracture, has been overcome. In our own clinic, we vary this with the urgency of getting the

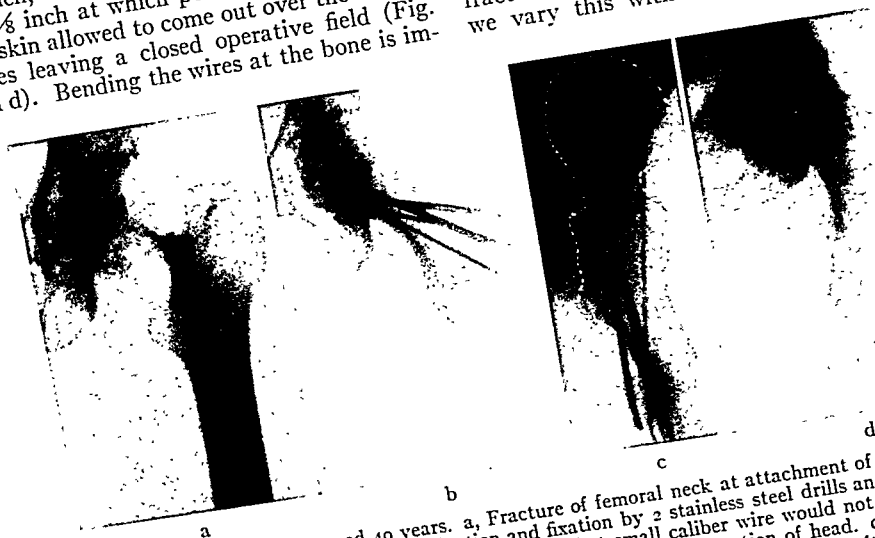


Fig. 8. Case 5. Female, aged 49 years. a, Fracture of femoral neck at attachment of head. b, Anteroposterior view immediately after reduction and fixation by 2 stainless steel drills and 2 Kirschner wires. Heavy drills used in this case because of fear that small caliber wire would not hold firmly in spongy capital bone since fracture is so proximal as to involve upper portion of head. c, Lateral view showing that one wire had missed the fracture line entirely. The other wire had made exit from neck but re-entered head. Two pins are well within femoral neck throughout. This picture illustrates the importance of final lateral views in all cases so that useless wires may be withdrawn and replaced. d, X-ray film made after 6 months showing evidence of bony union. Pins and wires removed earlier than usual because of irritation caused by the pins. Local infection and periostitis followed removal of pins. This is the only case in a series of 23 in which heavy pins were used and the only case in which infection occurred.

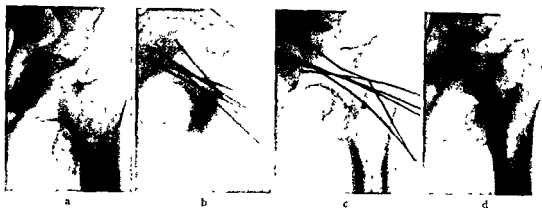


Fig 9 Case 6 Male, aged 62 years. a, Comminuted intertrochanteric fracture, left hip b, Anteroposterior view after reduction and transfixion by 5 Kirschner wires. Upper wire inserted too far and slightly retracted before clipping. Lateral view in this case showed 4 wires completely within the femoral neck, the fifth leaving the neck

but re-entering the head causing result shown in Figure 9d c, X-ray film taken after 6 months showing firm bony union. One wire, apparently the one which made exit from the femoral neck, being bent d, Roentgenogram taken 8 months after injury and 1 month after the removal of the wires.

patient up immediately. If the patient is old and in poor general condition, no traction is applied. If young, strong, and heavily muscled, the maintenance of about 10 pounds of traction for 10 days to 2 weeks will probably be more comfortable for the patient.

As for the number of wires used, we have arbitrarily used 5 in this clinic because we have found that 3 wires will bend (Fig. 5b), while 5 wires never have in our experience. We ordinarily use stainless steel Kirschner wires leaving them in place from 8 to 10 months or even longer, dependent on evidence of union as shown by the roentgenogram. The longest period in this series

has been 14 months (Case 1). In no case have we observed x-ray findings of irritation in the host caused by the wires. As previously stated, we have found it safe to allow the patient up immediately in wheel chair, and after 6 to 8 weeks, on crutches. We have not allowed weight bearing until some evidence of union is present. When weight bearing is started, no inconvenience is caused by the presence of the wires under the skin except that in some cases the patients complain of a pricking sensation where the end of the wire was perhaps left unusually long or has become too long by extrusion, an event which occasionally takes place



Fig 10 Case 7 Female, aged 56 years a, Impacted fracture mid portion of femoral neck b, Same case immediately after transfixion by 5 crossed Kirschner wires. This case, requiring no reduction, was done on fluoroscopic table c, After 10 months and immediately after removal of Kirschner wires. X-ray evidence of firm bony union. Weight bearing, and symptom free for past 6 months



Fig. 11. Case 8. Male, aged 68 years. a, Anteroposterior view showing comminuted fracture through base of femoral neck and through trochanters. b, Immediately after reduction and after insertion of 4 wires. Two lower wires inserted too far and required slight withdrawal. Upper wire is the external guide wire. c, X-ray film taken

4 months after injury showing 5 wires in position. The cause of the bend in 1 wire is undetermined. d, Anteroposterior view 8 months after injury, and 2 weeks after removal of wires. Note that bony union is complete. Full weight has been borne since 3 months before removal of the wires.

A few rules or words of caution might be of value:

1. Reduction should be as nearly perfect as possible. Odds in favor of nonunion or absorption of head are in inverse ratio to accuracy of reduction.

2. Lateral x-ray checks are essential for reduction, of course, but also to check the wires. A wire which does not traverse the fracture line and stay within the femoral neck and head throughout its course in both the anteroposterior and lateral views is useless and should be removed and re-inserted. An exception to this rule is shown in Figure 8c; here a wire leaves the neck and re-enters the head.

3. To identify the wires on the film, it is helpful to clamp forceps of different shapes or preferably small lead markers to the Kirschner wires before roentgenograms are made.

In impacted hip fractures in good position there is a tendency on the part of many surgeons to leave well enough alone. In these cases we believe that wiring should always be done. If no reduction is necessary, the wires may be inserted quickly on the fluoroscopic table under direct vision with practically no shock and little inconvenience to the patient (Fig. 10). One does not then have to fear that the impaction will become loosened and the reduction be lost as happened to

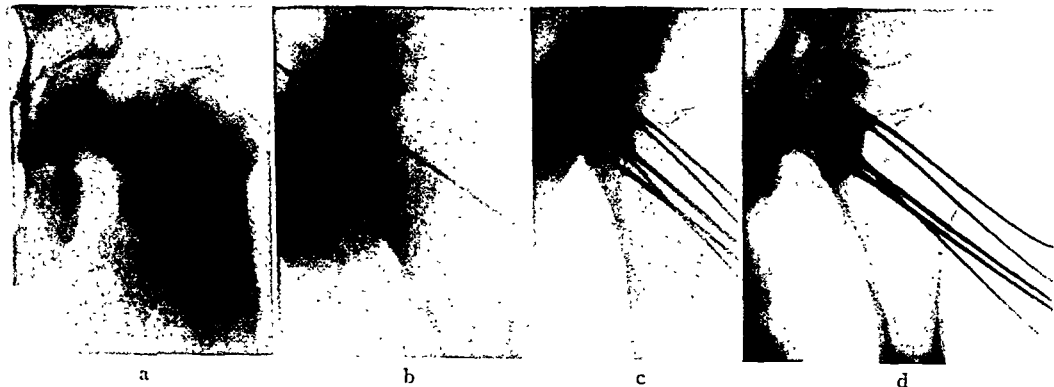


Fig. 12. Case 9. Female, aged 54 years. a, Comminuted fracture through distal portion of femoral neck. b, Immediately after reduction showing relation of external guide wire to normal line of femoral neck. Slight varus obtained in this case improves chances of bony union. c, After insertion of 5 Kirschner wires. d, After 5 months. X-ray

evidence of definite bony union is shown. There is no evidence of angulation, or bending of the wires, despite the fact that this patient weighed more than 200 pounds and was unrestricted as to movement. Full weight bearing is still prohibited at this time because of this excessive weight.

one of our patients several years ago (Fig. 2). Since this unfortunate experience, we have wired impacted hip fractures as a matter of routine.

As for use of the fluoroscopic table routinely in impacted cases, we do not recommend it unless one is fortunate enough to have a modern combined fracture fluoroscopic table. We believe that the ease of reduction and fixation of the patient on a good fracture table outweighs the advantages of fluoroscopy despite time wasted while waiting for development of repeated series of films. A portable fluoroscopic headpiece is perfectly useless in hip fractures. An additional disadvantage of the fluoroscopic technique is exposure of the operator which this method entails. Satisfactory methods of shielding the orthopedist's hands from the rays have yet to be devised, and so much unavoidable fluoroscopic work is necessary in a busy orthopedic clinic that whenever possible it should be avoided.

Roentgenographic case records are presented to illustrate special features of the technique. In their selection an effort has been made to include as many different types of hip fractures as possible (Figs. 4 to 12).

#### CONCLUSIONS

Further data with reference to the multiple Kirschner wire method of treatment in hip fractures are presented. Cases illustrating various types of hip fractures are demonstrated.

The writer has used this method in 23 patients over a period of  $3\frac{1}{2}$  years. Five are under treatment and cannot be classed as cures, but all show x-ray evidence of union. Eighteen patients are cured. There has been 1 case of infection in which 2 nails and 2 wires were used (Case 6). The ultimate outcome of this case must be classed as doubtful. No case of nonunion has occurred.

The relative simplicity of this method and uniformly good results possible under proper application together with minimal surgical shock warrant a more thorough test and widespread use.

Photography by U S Army Signal Corps, Fort Sam Houston, Texas

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# A ONE STAGE OPERATION FOR THE CURE OF CARCINOMA OF THE AMPULLA OF VATER AND OF THE HEAD OF THE PANCREAS

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THE operative story of growths in the region of the head of the pancreas and in the second portion of the duodenum is of great interest to all physicians and surgeons both because of its constant challenge and because at the present time the only effective operation shuts off permanently the external secretion of the pancreas without apparent significant effect upon the health of the patient. This story, although commenced in 1888, has not been one of rapid progression toward successful removal characteristic of many other abdominal operations for malignant growths since that date. Factors obviously responsible for this delay are, as stated by Judd and Hoerner, (1) the insidious onset of the disease, (2) the generally poor condition of the patients, (3) the relative inaccessibility of the lesions, (4) the proximity of important structures which cannot be sacrificed, and (5) the extreme technical difficulties of the procedure. Although the operation here described was performed to remove a carcinomatous growth arising from Vater's ampulla, the same operative technique may be applied to other tumors in this whole periampullar area whether they arise from the duodenal wall, the common duct, the pancreatic duct, or the head of the pancreas.

That carcinoma of the ampulla of Vater is insidious in its onset is well known, and a positive diagnosis is a matter of great difficulty and has comparatively seldom been made before operation. There is no pathognomonic nor even any constantly recurring symptom, although jaundice is by far commonest. This is usually gradual in onset and progressive, although there may be a distinct intermittency (due probably, as Outerbridge suggests, to turbulence and vascularization of the neoplasm) as opposed to carcinoma of the pancreas in

which the jaundice is more apt to be steadily progressive.

Associated conditions such as pruritus will, of course, accompany or follow the jaundice. This was the first and for several months the most distressing symptom in the case here reported. Afterward come anorexia, rapid loss of weight, and more or less pronounced decoloration of the stools, amounting in some instances to complete acholia. Next in frequency, in approximately one-half the cases, comes pain, either in the epigastrium, gall bladder, liver region, or back.

The conditions with which cancer of Vater's ampulla is most likely to be confused are obstruction of the common duct by stone, benign stenosis from scar formation, chronic interstitial pancreatitis, and cancer of the head of the pancreas. Expectant treatment of some of these conditions may be wise; but to temporize too long or to split hairs in attempting to establish a diagnosis in the presence of a malignant growth at the ampulla of Vater may render removal impossible because of extension or metastases, or may make the patient, because of the harmful consequences attendant on biliary obstruction, a poor or prohibitive operative risk. Metastases are rarely found in a patient with cancer of Vater's ampulla; this fact is of course favorable and is a stimulus toward attempted operative cure. On the other hand, this freedom from metastases is also indicative of an unfavorable fact—that a patient with such an obstruction of the biliary and pancreatic ducts succumbs rapidly, too soon for metastases to occur. The average duration of life in 47 cases studied by Outerbridge was only 7½ months; in 23 cases it was less than 6 months; and in 10 cases less than 3 months. Upcott writes: "There is probably



teric, and splenic veins; the abdominal aorta; the splenic artery; and the origin of the superior mesenteric artery.

Anteriorly the pancreas is covered with the peritoneum of the omental bursa, which separates it from the overlying stomach, transverse colon, and transverse mesocolon. Just at its superior surface is the celiac axis and its branches; its inferior surface is in contact with the transverse portion of the duodenum and the duodenojejunal flexure (Fig. 1).

The secretion of the pancreas in man is quite abundant, being 500 to 800 cubic centimeters a day, and its digestive action depends upon its three groups of enzymes—proteolytic, amylolytic, and lipolytic. Evidently the proteolytic enzyme of the juice is secreted in a zymogen or pro-enzyme form (trypsinogen), which is activated or converted to trypsin by something contained in the mucous membrane of the small intestine (duodenum, jejunum). Pavlov supposed this substance to be an enzyme, and called it kinase or enterokinase, which by hydrolytic action upon the trypsinogen converts it into trypsin. Trypsin acts with another important proteolytic enzyme of the pancreas, crepsin, to split the protein molecule into its constituent aminoacids.

The starches are acted upon by the diastatic enzyme (amylase), which is found in the secretion of the pancreas or in an extract from the gland. Its action is similar to, or identical with, that of ptyalin, causing a hydrolysis of the starch, with the production of maltose and acro-odextrin. Before absorption these substances are further acted upon by the maltose of the intestinal secretion and converted to dextrose.

The third important class of enzymes in the pancreatic juice attacks neutral fats through an active enzyme, lipase, capable of hydrolyzing or saponifying these fats, breaking them up into glycerin and the constituent fatty acid. It should be added that the action of this enzyme is aided very materially by the presence of bile. Although this latter secretion contains no lipase itself, nevertheless mixtures of bile and pancreatic juice split the neutral fats more rapidly than does pancreatic juice alone.

Faced with a growth at the ampulla of Vater obstructing the common duct, the surgeon has the choice of three operative procedures: (1) leaving the growth in place and short-circuiting the flow of bile by an anastomosis between the common duct or gall bladder and the stomach or intestine; (2) incision of the duodenum, local removal of the growth, and fixation of the stumps of the common and pancreatic ducts to the duodenum at the same area from which the tumor was excised; (3) radical removal of the growth by resection of the first and second portions of the duodenum. Continuity of the gastrointestinal tract must then be re-established by an anastomosis between the stomach and the jejunum, and of the biliary tract by an anastomosis between the stump of the common duct or the gall bladder and the stomach or intestine. Neither of these procedures restores the channel of the pancreatic duct for the flow of bile into the intestine, and the re-establishment of this flow has been the most baffling problem to the surgeon, the real *bête noire* which has been the cause of operative timidity and of consequent delay in the surgical answer to this whole question. Attempts at such a reconstruction, after a sufficiently wide resection of the tumor, have resulted in a high incidence of leakage of both pancreatic and duodenal secretions, with the resulting prohibitive mortality.

Operations for diseases of the pancreas itself preceded by 10 years those for a tumor at the ampulla of Vater, but those paved the way for these because the field and the operative principles involved in each operation are primarily the same. The ingenuity, courage, and technical skill of the pioneers in the work are manifest to everyone reading their reports.

Sauvé, in an article on this whole problem published in 1908, stated that Mayo-Robson at the Congrès de Paris in 1900 credited Billroth with having removed the entire pancreas because of its involvement in a growth, with recovery of the patient; this was in 1884. Since no operative details of the case were available, however, Sauvé subtracted this case from his report. He included 8 other cases of resection of the head of the pancreas, those of Ruggi, 1889; Terrier, 1892; Kroen-



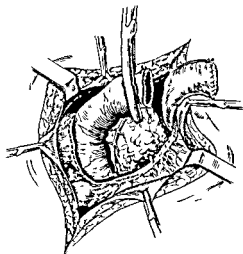


Fig 2 Transection of duodenum between first and second portions. Mobilization of duodenum by incision along Wirt's line (After Sauvé, *Rev d chir*, 1908)

lein, 1893; Biondi, 1896; Sendler, 1896; Tricomi, 1898; Codivilla, 1898; Franke, 1901. To these 8 he added 3 other cases, those of Tuffier, 1905; Michaux, 1906; and Duval, 1906. In 5 of these 11 patients an isolated benign tumor in the pancreas was resected, 3 of the patients recovered; and in 2 there was local resection of the pancreas for carcinoma; both patients died of metastases after 4 months. The 4 remaining patients had combined operations. Duval's patient was well 9 months after resection of the pyloric end of the stomach, which contained an ulcer perforating into the pancreas, resection of pancreatic tissue about the ulcer, and a posterior gastroenterostomy. Michaux removed the second and third portions of the duodenum with the contiguous pancreatic tissue, left the first portion of the duodenum together with the common duct intact, and performed an anterior gastroenterostomy, the patient died that same day of shock. Tuffier excised the head of the pancreas, ligating the common duct and performing a cholecystoduodenostomy; the patient died 24 hours later. Codivilla performed a most interesting operation for which he is entitled to great credit. Finding a cancerous process in the head of the pancreas which could not be separated from the duodenum, he resected *en bloc* the head of the

pancreas, a major portion of the duodenum and the pyloric end of the stomach, re-established the gastrointestinal flow with a Y-gastroenterostomy after the method of Roux, and with a Murphy button added a cholecystenterostomy. The patient lived for 24 days, dying with progressive cachexia and glycosuria.

The operative attack on growths situated directly at the papilla of Vater began in 1898 when Halsted, encountering a greatly dilated common duct and feeling a small hard growth at the ampulla, opened the duodenum, excised a V-shaped section of the duodenum, including the growth and the first portion of the common and pancreatic ducts, and closed the duodenum, implanting the stumps of both ducts into the suture line of closure. His patient lived free of symptoms for 7 months, then died with a recurrence of original growth.

Early in the operative story came the suggestion of a two stage operation, a suggestion which was founded on the belief that such obstructive symptoms as cholemia should be relieved by a less serious operation before radical extirpation of the tumor is attempted. Procedures of this sort were reported by Mayo in 1901 and Kausch in 1909; the former's first operation was a cholecystostomy, the latter's a cholecystenterostomy.

The two stage attack was likewise recommended by Sauvé in 1908 in describing an operation for resection of the head of the pancreas which he had conceived by dissection of fresh cadavers. At the first stage a gastroenterostomy was made, Sauvé calling this first stage "la reconnaissance en force avant la bataille." He advised against forming the new path for the bile flow at this stage because this procedure would mask the operative field of the second stage. At the second stage the second portion of the duodenum together with the adjacent pancreatic tissue was resected and the bile flow was re-established by a choledochenterostomy. Sauvé regarded this latter procedure as far preferable to a cholecystenterostomy or a cholecystgastrostomy since these two operations predisposed the patient to an angiocholitis of intestinal origin. Then Sauvé came to a prophetic conclusion when, in discussing the treatment of the remaining pancreatic

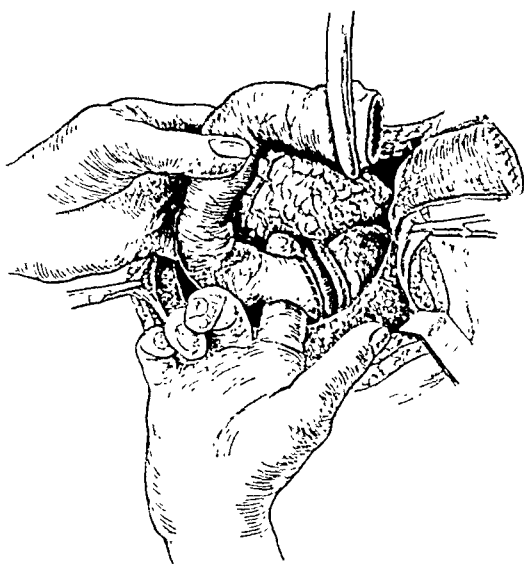


Fig. 3. Duodenum and head of pancreas freed. Superior mesenteric vessels isolated. (After Sauv , *Rev. d. chir.*, 1908.)

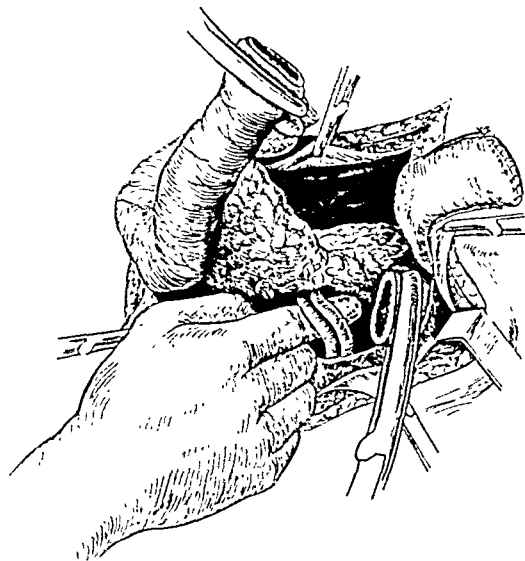


Fig. 4. Distal stump of duodenum brought out from under superior mesenteric vessels preparatory to closure of stump. (After Sauv , *Rev. d. chir.*, 1908.)

stump, he pointed out the impossibility of suturing the duct of Wirsung directly to the intestine and condemned the attempt to graft the pancreatic stump into the intestinal canal. He ended the speculation about this problem by concluding that it is necessary to resign oneself to the loss of the external function of the pancreas. "Il faut donc se r signer   la perte de la fonction externe de la glande." As if such a departure seemed too radical, he added a last paragraph to say that to avoid fat necrosis it might be best to place drains down to the stump of the pancreas in order deliberately to form a pancreatic fistula (Figs. 2, 3, 4).

For the next 30 years no significant addition was made to the surgical treatment of lesions in the head of the pancreas or in the duodenum at the ampulla of Vater. Growths in the latter site, if attacked surgically, were treated by a transduodenal incision with a local removal after the manner of Halsted, although Koerte in 1904 tried a slightly more radical removal of the cancer by a circular resection of a small area of the duodenum just at the ampullary region, making an end-to-end anastomosis of the duodenum and implanting the common and pancreatic ducts

into the suture line. His patient survived the operation only a few hours.

In 1905 Moynihan, in discussing operations for malignant disease of the pancreas, wrote: "I have elsewhere collected the records of all cases operated upon—13 in number. They all serve to show that the mechanical difficulties of the operation are well-nigh insuperable, and that if boldness and good fortune are the operator's gifts, the result to the patient hardly justifies the means."

Geiser in 1906 made a complete analysis of the subject of malignant disease of the duodenum, including all tumors of the ampulla of Vater, no matter what their histological origin, and collected 51 cases, of which 19 were operative, of what he called "periampullar" carcinoma.

To support the surgical attack on the pancreas, Coffey in 1909 devised in experimental animals an ingenious but rather complicated operation. He believed that the surgeon was fearful of operations involving the human pancreas because it was devoid of peritoneum, and that, although the fat splitting enzyme had been the dread of surgeons up to that time, there was no evidence that it would penetrate the peritoneum to a serious extent.

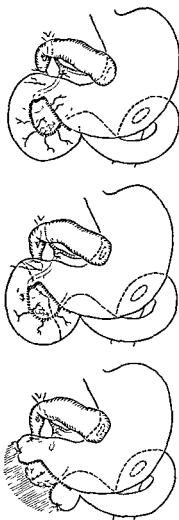


Fig 5 Operation of Whipple, Parsons, and Mullins 1935

This was a two stage operation the scheme of which was to implant the stump of the pancreas into a loop of intestine, effecting a peritoneal covering for this stump by invaginating it into the intestine.

In 1913, after an extensive search of the literature, Outerbridge added 59 cases of perianal carcinoma to the 51 Geiser reported, making a total of 110 available for analysis.

That the operative mortality continued high is borne out by the figures of successive investigators. In 1927 the report of Cohen and Colp of 59 cases of radical operations for

carcinoma of the perianal region represented their complete summary of the literature from 1898 to 1925, the operations being mostly transduodenal excisions with reimplantation of the common duct into the suture line, and some with reimplantation of the head of the pancreas into the duodenum. They reported a gross mortality of 43 per cent in 59 instances in which a variety of operative procedures was employed, and stressed the fact that even in two stage operations the risk of establishing external biliary drainage by some type of anastomosis between the biliary and upper intestinal tract in the presence of obstructive jaundice is not negligible, and that many patients subjected to such a procedure have not survived to undergo a radical excision of the growth.

In the same year, 1927, Fulde reported 52 operative cases with a mortality of 42 per cent. In 1931 Mueller and Rodemaker stated that the mortality rate of surgical procedures in this area was 30 to 70 per cent, depending on the duration of the jaundice and the type of operation performed.

In 1935 Whipple, Parsons, and Mullins added 20 reported cases to the 59 collected by Cohen and Colp, and described their two stage operation for carcinoma of the head of the pancreas. In 1935 also, Hunt and Budd collected 76 cases in which patients were treated surgically, including 18 cases between 1925 and 1934; the gross mortality was 39.77 per cent. In 1937 both Cooper and Brunschwig published reviews of the subject, and the latest report is by Kafka, a comprehensive review of all cases of perianal carcinoma from 1900 to 1939. The results of operation in 115 patients are presented in Table I.

TABLE I—RESULTS IN 115 CASES

	Exclusions	Resections	Total
Number of operations	94	21	115
Operative deaths	32	10	42
Per cent operative mortality	34	47.6	36.5

This brief review of the anatomy, the physiology, the clinical course of patients suffering from pathological conditions in this area, and the operative efforts to cure these conditions makes it clear why the region about the head of the pancreas has until now

been regarded by surgeons as a forbidden territory. The well conceived, if unsuccessful operation of Codivilla in 1898, the prophetic statement of Sauv  in 1908, and the successful operations reported by Whipple and his co-workers in 1935 have cut the Gordian knot which tied in fear the venturesome but conscientious operators for so many years. It now seems apparent that it is not necessary to attempt the hazardous procedure of re-establishing the flow of the external secretion of the pancreas into the intestine, and that a person may remain in good health without the digestive enzymes hitherto thought indispensable. There is, moreover, the possibility that the pancreas possesses, in addition to insulin, other internal secretions which aid in the metabolism of the fats and proteins and which are sufficient to maintain normal metabolism after all external secretions are blocked by ligation of the pancreatic ducts. This theory seems to coincide with the discovery of Dragstedt and his co-workers of a specific substance in alcoholic extracts of beef pancreas which on oral administration to depancreatized dogs treated with insulin permits survival and prevents the fatty degeneration and infiltration of the livers of these animals. This substance, for which the name "lipocaic" was suggested, is believed to be a new hormone that is concerned in some way with the normal transport and utilization of fat.

This same hypothetical internal secretion of the pancreas was thought by Boyce to explain the ability of dogs to digest an unusually high fat and protein diet after the exclusion of the pancreatic ducts from the intestinal tract but with the pancreas itself left undisturbed.

When, in 1935, Whipple, Parsons, and Mullins described their operative attack on carcinoma of the head of the pancreas they stimulated surgeons to new effort and revived flagging hopes. This operation was a radical excision *en bloc* of the tumor by a two stage procedure. In the first stage the patient was subjected to a gastroduodenostomy, ligation of the common duct, and cholecystgastrostomy; in the second stage, to an excision *en bloc* of the second portion of the duodenum includ-

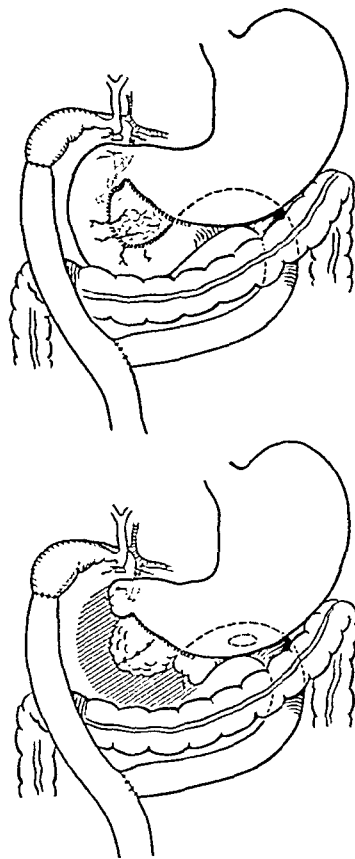


Fig. 6. Operation of Whipple. 1938.

ing the ampulla of Vater, the lower common duct, and the surrounding portion of the head of the pancreas, with permanent ligation of the pancreatic duct and stump (Fig. 5).

This operation, although admirable in many ways, has certain objectionable features, some of which have already been eliminated by its authors. In the first place, an ascending cholangitis developed some months later in a number of patients subjected to this procedure, which was due apparently to the entrance of secretions from the stomach into the gall bladder directly through its line of anastomosis with the stomach. In 1908 Sauv , as stated before, made this observation and maintained that there would be less danger of retrobiliary inflammation if the gall bladder or the common duct was anastomosed to the duodenum or to the jejunum



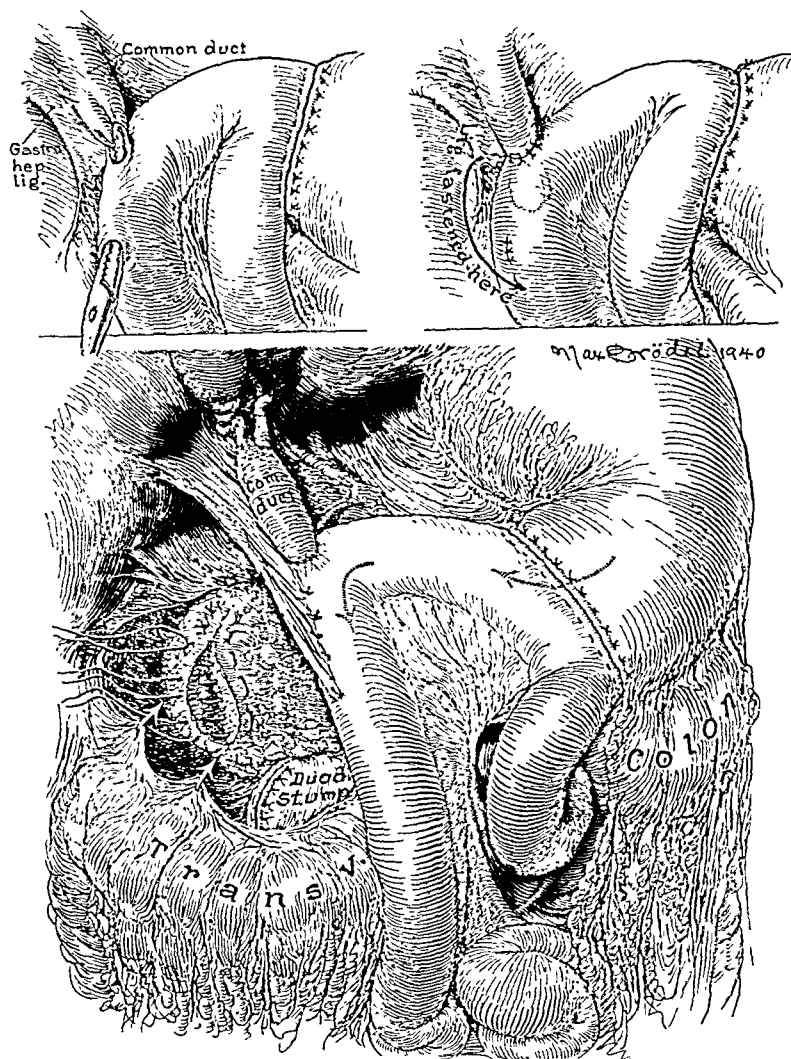


Fig. 8. This shows the suture of the pancreatic stump, including the pancreatic ducts, and the implantation of the stump of the common duct into the jejunum.

probability this is due to necrosis of the thin walled avascular common duct at the point of ligature, which is also the cause of the temporary leakage of small amounts of bile around the cigarette drain inserted down to the ligated stump of the cystic duct after the usual cholecystectomy. In our operation we avoided this complication because, instead of leaving a ligated blind stump of the common duct, we anastomosed the open end of the common duct directly to the intestinal tract.

One other objection which may be raised to resections in this area, as previously carried out, is that, whereas the second portion of the duodenum was resected, the first was left in place closed over as a blind stump, and the patency of the gastrointestinal tract was restored by a gastroenterostomy. This proximal duodenal stump forms an additional suture line and, therefore, an additional potential point of leakage. We have avoided this difficulty by resecting the entire first

portion of the duodenum as well as the second portion and also the pyloric end of the stomach, and by restoring the gastrointestinal flow by one suture line only, an end-to-side anastomosis between the jejunum and the distal end of the stomach, the so called anterior Pólya anastomosis. This procedure has the additional great advantage of bringing the jejunum high up under the edge of the liver where the stump of the common duct may be anastomosed to it without tension.

A final objectionable feature to the operation as previously carried out arose from its performance in two stages, and this objection we have attempted to eliminate by our single stage attack. Many times after the performance of the first stage of a planned two stage operation, the patient, greatly improved by the re-establishment of the biliary flow, is lulled into a sense of false security and is unwilling to undergo the second operation. The chief argument of the proponents of a two stage procedure is the restoration of the flow of the bile into the intestinal tract by the first operation, thus enabling the patient better to withstand the subsequent resection, with less tendency to hemorrhagic manifestations so common to all forms of obstructive jaundice. This seems a reasonable tenet, particularly in very ill or in elderly patients in whom a two stage performance of an operation may prevent the whole of the operative shock from equalling the sum of all its parts. However, the present use of vitamin K has reduced the hazard of hemorrhage, thereby rendering some of these very ill patients justifiable risks for an operative procedure in one stage. The chief advantage of a one stage performance is that all the work is done in a clean operative field as opposed to a field masked and obscured by trauma of a preliminary operation. With so many vital structures in so small a space, complete differentiation is difficult but imperative in order to avoid injury to these structures and to effect the delicate restorative anastomoses. Many times at the second operation in a two stage performance the adhesions are so dense that removal of the growth at the head of the pancreas is found impossible. We believe, therefore, that the excision of a carcinoma situated

in this region will be attended with the greatest chance of success if the operation can be done in one stage after the patient has received proper vitamin therapy and is given a large transfusion at the very beginning of the operation, which is allowed to run continuously during entire course of the operation.

#### CASE REPORT

M. McF, a white woman, aged 42 years, complained of severe pain beneath the lower end of the sternum, fever, and jaundice. Her father was alive but suffered with diabetes. She had always had excellent health.

In September, 1939, an attack of intense pruritus developed which continued 11 weeks, it was not accompanied by jaundice or any other symptom. Following the subsidence of this attack, about the middle of December, 1939, she was well until March, 1940, when the pruritus returned and was soon followed by an obstructive type of jaundice, but no pain. She was a patient in the Johns Hopkins Hospital for a period of 2 weeks at this time, from March 23, 1940, to April 6, 1940, when on examination she was found to be physically sound except for the jaundice and an enlarged left kidney. The blood count showed a microcytic, hyperchromic anemia. The red blood cells numbered 4,420,000, the hemoglobin was 9.3 grams (64 per cent), and the white blood cells, 5,580. The blood analysis showed cholesterol 417 milligrams per cent, sugar 91 milligrams per cent, nonprotein nitrogen 34 milligrams per cent, and the van den Bergh a delayed biphasic reaction, 2.0 milligrams per cent. The stools were clay-colored and gave a positive guaiac and benzidine reaction. The urine was deeply pigmented by bile. Roentgenograms of the stomach and gastrointestinal tract revealed no abnormality, those of the gall bladder showed failure to concentrate the dye. The jaundice diminished while she was in the hospital and she was discharged untreated April 6, 1940, with the diagnosis of catarrhal jaundice.

Following her return home the itching and jaundice persisted. Suddenly in the morning of April 25, 1940, she had sudden severe pain high up in the epigastrium running up beneath the sternum, was nauseated, and vomited. The pain remained severe. She was seen that same afternoon in consultation at the request of Dr. John W. Parsons and admitted to the Church Home and Infirmary.

Examination showed a well developed, well nourished woman of 42 years who was suffering with abdominal pain. The temperature was 100.6 degrees, the respirations were 18, and the pulse was 90. There was a definite icteric tint to the skin and sclerae. The lymph glands were not enlarged. The lungs were clear. There was a loud systolic murmur at the apex of the heart. The abdomen showed restricted motion in the right upper quadrant where there was some tenderness and muscle spasm, but

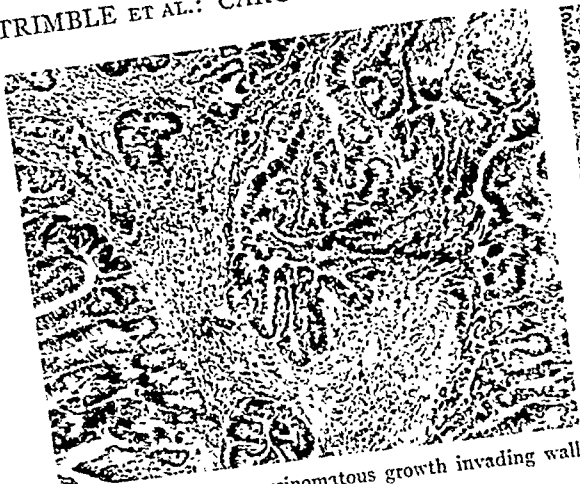


Fig. 9. Papillary carcinomatous growth invading wall of duodenum.

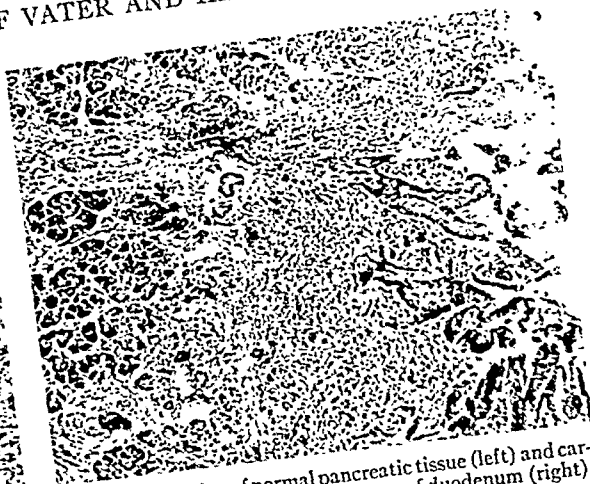


Fig. 10. Junction of normal pancreatic tissue (left) and carcinomatous tissue from ampullary area of duodenum (right).

no definite mass could be felt here. The blood showed 28,000 white blood cells; hemoglobin, 82 per cent; icteric index, 30; and Kahn test, negative. The urine was deeply pigmented with bile but showed no sugar or albumin; the voided specimen contained a few red and a few white blood corpuscles (the patient was menstruating).

On April 26, 1940, the day after admission to the hospital, since her temperature had risen to 103 degrees, and since the abdominal symptoms had not abated, after consultation with Drs. J. W. Parsons and W. A. Baetjer, she was subjected to operation. A needle was introduced into the antecubital vein of the left arm and a 5 per cent dextrose solution in normal saline was allowed to run slowly during the entire course of the operation. Anesthesia was induced with nitrous oxide and oxygen and continued with drip ether on the open mask by Dr. S. Griffith Davis. Through a high right rectus incision an enlarged, tense, smooth walled gall bladder was found that could not be emptied by pressure. The cystic duct was very small. The common bile duct was greatly dilated, measuring 1.5 centimeters in diameter; seropurulent fluid was aspirated from this duct and Gram positive diplococci were found on smear. No stones could be palpated in either the gall bladder or the common duct. A soft round tumor mass could be felt within the second portion of the duodenum. Through a small longitudinal incision in the duodenum this mass was seen to be a papillary growth 3 centimeters in diameter surrounding the ampulla of Vater which by frozen section proved to be adenocarcinoma.

It was decided to resect this growth with its duodenal, choledochal, and pancreatic connections. The duodenum was mobilized and divided between the clamps at the distal end of its second portion. The resected duodenum was reflected to the right, the head of the pancreas removed with it, and in the same block the distal 5 centimeters of the stomach. The first and second portions of the duodenum to-

gether with the pyloric portion of the stomach, the distal end of the common duct, and the head of the pancreas were then resected *en masse*. All bleeding points were ligated, catgut being used because of the organisms found in the material aspirated from the common duct. The cut surface of the pancreas was transfixed with mattress stitches of catgut. The distal stump of the duodenum was turned in with a continuous double row of No. 6 chromic catgut, and this closure was reinforced with a layer of mattress sutures of fine silk. A loop of jejunum about 30 centimeters from Treitz' ligament was brought anterior to the transverse colon and sutured to the open stump of the stomach, after the anterior Pólya method. The stump of the common duct was implanted into the side of the jejunum about 20 centimeters distal to the site of the gastroduodenostomy. This step was accomplished by first making a small incision in the jejunum distal to the proposed site of implantation, placing a Kelly clamp within the bowel and out through the jejunum at the proposed site, drawing the stump of the common duct into the duodenum, and suturing the duct to the proximal opening in the jejunum with interrupted stitches of fine silk. This procedure was effected only after some difficulty because of the extreme thinness of the walls of the common duct. The line of anastomosis was reinforced by stitching omentum about the suture line. The distal opening into the jejunum was closed with interrupted silk stitches. One cigarette drain was inserted into the lesser peritoneal cavity and one placed down to the anastomosis between the common duct and the jejunum. The deeper layers of the wound were closed with catgut and the skin was closed with silk. The patient received 500 cubic centimeters of blood during the latter part of the operation through the intravenous cannula already in place. She withstood the long procedure very well; at the close of the operation the pulse was regular at 120 beats a minute and blood pressure was 110/75 (Figs. 7, 8, 9, 10).



The patient recovered rapidly from the operation. There was no vomiting, no pancreatic or biliary drainage after the first few days, and no digestive discomfort or fatty stools. Pancreatic enzymes given by mouth proved distasteful and were stopped. On the sixteenth postoperative day she suffered a rather severe hemorrhage of undetermined origin, vomiting blood and losing some blood from the abdominal wound. Thanks to the alertness of Dr. Howard Jones and his staff at the Church Home and Infirmary she received a transfusion within a few minutes after the onset of the hemorrhage. After that she improved rapidly and was discharged from the hospital on June 2, 1910, 5 weeks after operation.

She returned a month later to her position as secretary and stenographer, where she works 8 hours a day. She has gained 15 pounds. There has been no digestive disturbance except once or twice a transient vague epigastric discomfort after eating the fat in ham, and no abnormality in the stools. These are well formed and of a normal consistency and color, showing no evidence at any time of steatorrhea. Serum lipase estimation was made on January 8, 1911, 9 months after operation, after the method of Comfort and Osterberg, and found to be 1.47, expressed in cubic centimeters of twentieth normal sodium hydroxide solution. The serum diastase was determined on the same date by the glycogen cleavage method, expressed in cubic centimeters of thiosulphate solution required in the titration of the maltose formed by incubating the serum with 1 per cent glycogen solution. This was 0.745 cubic centimeters. These two determinations are believed to be within the limits of normal.

In answer to a letter which we wrote to Dr. A. O. Whipple on October 22, 1910, telling him of our patient who was subjected to operation on April 26, 1910, he sent a very courteous reply describing a patient of his in which much the same operation as ours was employed. The first patient was operated on by him on March 6, 1910, and is in excellent health except for the necessity of taking pancreatic extract to avoid the loss of too much fat in her stools. His second one stage procedure was done in October 1910, the patient died in 6 days of an overwhelming lobar pneumonia.

#### SUMMARY

1. The difficulties of a surgical attack upon the ampullary region of the duodenum and the head of the pancreas are outlined.

2. A brief survey of the operative story is given.

3. A one stage operation for the cure of carcinoma in this area is described together with a clinical report of the case.

4. In this patient the deprivation of the pancreatic secretion by permanent ligation of the pancreatic duct has for the past 11 months had no apparent effect upon the digestion of fat, carbohydrate, and protein.

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# SLIPPING OF THE UPPER FEMORAL EPIPHYSIS

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NO altogether satisfactory name has been devised to include all phases of this disease. The terms epiphyseolsthesis and epiphyseolysis are perhaps suitable for expressing the condition of the epiphyseal disc at two stages, but do not include the earliest and latest stages nor the changes in the soft tissues. The terms *preslipping* or *slipping* of the upper femoral epiphysis will be used here for the sake of convenience.

A study of 70 cases of this condition from the New York Orthopaedic Hospital was presented 8 years ago.<sup>1</sup> Sixty-two additional patients have been treated since that time, a total of 132. The statements made in the present report are based upon a careful and complete analysis of all of these cases seen personally. Detailed statistics and tables will be omitted, but are available.

## ETIOLOGY

The incidence was slightly greater in boys than in girls, possibly due to the greater activity of the adolescent boy. The condition was bilateral in one-fifth of the first group but in only one-fifteenth of the second. This difference is probably explained by the earlier diagnosis in the latter group, with attendant protection of the second hip. The right hip was involved in 38 per cent, the left in 48 per cent, while 14 per cent were bilateral. Only half of the children were of the endocrine type, but 65 per cent were tall or overweight. It is difficult to explain this disease on a purely endocrine basis as at least half of the children were not of the endocrine type, and it is preponderantly unilateral. Tonsils had been removed at, or shortly before, onset in half of the cases, and other foci of infection were present in 20 per cent. Trauma of sufficient degree to cause an epiphyseal displacement was rarely present. Trauma was absent at the onset of most of the cases, and when

present was usually trivial, such as stepping off the curb. Frequently the patient dates the onset from some minor injury, but in almost every case there were symptoms before the injury. It is certain that trauma is not the primary cause of the disease, but rather a frequent incident in its course.

## STAGES

There are four stages of the disease, although there often may be no sharp division between them. They are the *preslipping*, *slipping*, *quiescent*, and *residual* stages. The existence of the *preslipping* stage has been denied, but there is abundant evidence to support its existence. It may not be seen when the child does not seek early medical care, or when this stage is not recognized by the physician. Nineteen of these cases had definite symptoms, signs, roentgenographic changes without evidence of slipping in anteroposterior and lateral roentgenograms, and pathological changes upon exposure of the hip at operation. Slipping subsequently occurred in 2 of them, whereas in the others the evidences of disease disappeared after operation. The *slipping* stage may begin suddenly or gradually, and the slipping may continue for several months. The condition is *quiescent* when the symptoms and signs have subsided and the roentgenogram shows a healed epiphyseal line. It is *residual* when there is complete bony union at the line.

## ONSET

The age at onset of the *preslipping* stage was 9 to 16 years, the average 12 years. The onset averaged 18 months earlier for girls than boys. The age at slipping was 10 to 17 except in 2 frankly traumatic cases, aged 8 and 9 years. The average age for slipping was 13.5 years. The age for slipping was 2 years younger for girls than boys. The interval between onset and slipping averaged 1 year, and the interval tended to be shorter in the older children.

From the New York Orthopaedic Dispensary and Hospital.  
<sup>1</sup>J. Am. M. Ass., 1931, 97: 1867.

## PRESLIPPING STAGE

The onset of the preslipping stage is usually gradual and vague. Every patient complained of a limp or pain, and most of them mentioned both. Usually there was some disability for vigorous activities, such as athletics. A minority noticed limitation of motion, weakness, and easy fatigability. The limp was also noticed upon examination, and varied in degree and protectiveness. Internal rotation, adduction, and often flexion were almost always found to be slightly limited, with pain and spasm at the extremes. The other motions were occasionally limited. The motions are grouped together for simplicity, and an index used expressing approximately the total percentage. An index of 90 to 110 represents normal motion. The index of motion in these cases ranged from 65 to 100, averaging 77. Slight atrophy of the thigh was common.

The leucocyte count of the blood was ten to twelve thousand in half of the cases, but the polymorphonuclear percentage was not increased. The erythrocyte sedimentation rate was above 10 in 90 per cent of the cases, and as high as 40, averaging 25 millimeters. Tests for syphilis and tuberculosis were uniformly negative.

The roentgenographic features were widening and irregularity of the epiphyseal line, with decalcification of the proximal end of the neck. The head was not visibly affected. The capsule was usually swollen.

## SLIPPING STAGE

In some cases there is a sudden slip, accompanied by aggravation of symptoms and signs. In extreme cases the patient is unable to bear weight on the hip, and has severe pain, spasm, and limitation of motion. The slipping is so gradual in other cases that no change is noted in the symptoms.

The roentgenogram reveals the degree of slipping. The typical deformity is a downward and backward displacement of the head with adduction (varus). There is only the posterior displacement in some cases, while in others the downward displacement is much greater than the posterior. The degree of posterior displacement may best be seen in the

lateral view. Callus forms in the inferior and posterior interval between the head and neck and may be seen soon after the slip. In many cases two or more layers of callus may be seen, indicating that two or more slips have occurred.

As the lesion becomes quiescent in either the preslipping or slipping stage, the epiphyseal line begins to assume its normal width and regularity, and the proximal end of the neck recalcifies. The callus soon becomes mature. The proximal margin of the neck superiorly loses its angular appearance and becomes smooth and level with the head. In younger children this smoothing and leveling of the neck may go so far as almost to obliterate the deformity of the slipping, leaving only a *cova vara*. After several months or years, depending upon the age of the patient, the epiphyseal line becomes ossified, thus reaching the residual stage at about the age of 16 in girls, 18 in boys. When there is much displacement, arthritic lipping at the margin of the head usually supervenes, and later it may involve the acetabulum. Downward displacement of the head is more serious than a posterior one in producing limitation of motion and arthritic changes. Circulatory changes in the head are rarely seen when the head has not been separated from the neck by surgical means.

## PATHOLOGY

We have operated upon 17 hips in the preslipping stage and 53 which have slipped, at varying degrees and periods after slipping, a total of 70 hips. Thus there has been an opportunity to study at first hand the pathology of the soft tissues of these hips. There are in the literature a few reports of examinations of the femoral head and neck at autopsy or resection late in the disease. Reports of the pathology of the soft tissues are essentially lacking. In the preslipping stage the capsule was usually found to be edematous and thickened, the periosteum of the neck and the synovial membrane were almost always thick, red, softened, and vascular, with a tendency toward pannus formation. The synovia was often increased in amount. The cartilage of the head and bone of the neck were normal.

except for an occasional granular appearance at the junction. Often the softening of the epiphyseal disc could be felt with the instrument. Microscopic examination usually revealed edema and hypervascularity of the synovial membrane, with collections of small round cells about the small blood vessels. Cultures of the synovia and the soft tissues were consistently negative in all stages.

The soft tissues in those patients seen after slipping, presented an appearance similar to that of the preslipping stage. There was usually a fold of soft redundant synovial membrane in the angle inferiorly and posteriorly, and an early pannus. The displacement of the head on the neck could also be seen, but not even in those patients seen within a few days of slipping was there separation of the head and neck. There was always a layer of firm fibrous or cartilaginous tissue covering the exposed portion of the end of the neck and joining it to the cartilage of the head. There was usually firm union of the head to the posterior-inferior portion of the end of the neck. Usually the distal side of the epiphyseal disc was soft, but in the later stages it had become firm again, sometimes solidly ossified. The cartilage of the epiphyseal disc had in most cases almost entirely disappeared, but the adjacent layer of capital cortex appeared normal. It appeared probable that in some cases there was no sudden slip, but a gradual displacement through the plastic tissue at the junction of the neck with the epiphyseal disc. Callus in various stages of maturity usually filled the angle inferiorly and posteriorly between the head and neck. Microscopic examination soon after a slip showed a thickened, vascular and edematous synovial membrane similar to that of the preslipping stage. The membrane in the later cases was thickened, but sclerotic and somewhat vascular.

#### THEORY OF CAUSE

What is the cause of this condition? Is the slipping primary or does it follow a softening and weakening at the epiphyseal line? The disease is seen only in children between the ninth and eighteenth years, which is the period of rapid growth. Many of the children are overweight or overgrown. The epiphysis ap-

pears to be normal previous to the onset of symptoms. The early symptoms and signs are those of a synovitis, and a swollen capsule is found in the roentgenogram. The sedimentation rate is usually elevated. The gross and microscopic pathology is that of a mild synovitis. We have seen 19 cases with these findings before any slip occurred. It appears that the primary condition is a synovitis of the hip during the period of rapid growth, and that this lesion causes circulatory changes in the epiphyseal disc resulting in decalcification and softening. The slipping is merely the natural result of weight bearing or mild injury to the softened epiphyseal junction. The cause of the synovitis is not proved, though the clinical and pathological picture and the elevated sedimentation rate suggest infection. The negative cultures may be due to our technical inability to culture the organism or virus involved, or the failure to take the culture early enough.

#### RESULTS

*Methods of evaluation.* Our purpose in the treatment of this condition is to secure a painless hip free of limp, with full motion and full capacity for normal activity. Hence our results must be evaluated in terms of the normal hip symptomatically, functionally, and anatomically, on a long term basis. The motions are grouped together for simplicity in a formula which approximates percentage. Further, we must know the results in untreated hips for comparison with treated ones. We should also know the relation of deformity to function, the effect of the impingement of the exposed neck on the acetabulum, and the importance of changes in the head due to circulatory disturbance. Finally, osteoarthritis in the residual stage must be considered. Untreated patients often get good hips even with moderate deformity, and they do not get the secondary changes in the head which often follow reduction. The lesion always heals and the patient can eventually walk, regardless of treatment. Our evaluation must be much more exact. We shall consider the results in the various stages in reverse order.

*Treatment in quiescent and residual stages.* Correction of deformity is usually the



Fig 1. Male, aged 14 years a, Symptoms 1 month, head displaced downward  $\frac{3}{4}$  inch, moderately posteriorly, index of motion, 17. b, After reduction by strong traction. Double spica in abduction and internal rotation for 3

months c, Roentgenogram which was taken 9 years after reduction. This is the best hip which was reduced by strong traction, index of motion, 66, little deformity is present.

chief problem in these stages. This may be accomplished by osteotomy through the healed epiphyseal disc, through the neck, or below the trochanters. Subtrochanteric osteotomy is preferred, because there is less likelihood of secondary damage to the head. The disadvantage of this procedure is the difficulty of controlling the upper fragment when the hip is movable, because of the pull of the

psoas muscle. We have used the operation in 6 cases with fairly satisfactory results. This operation may sometimes be preferred to open reduction soon after slipping. It should, however, be postponed to the quiescent stage because of the probability of limitation of motion from the immobilization in plaster during the acute synovitis. Osteotomy is indicated when the deformity results in much

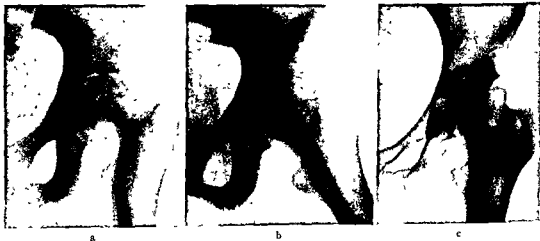


Fig 2. Female, aged 14 years a, Symptoms 8 months, index of motion, 11, head displaced downward,  $\frac{3}{4}$  inch and posteriorly, joint space thin, open reduction August

31, 1932 b, After removal of spica, 12 weeks after operation c, Head degenerated 3 years after operation, 7 $\frac{1}{2}$  years after operation, index of motion, 13

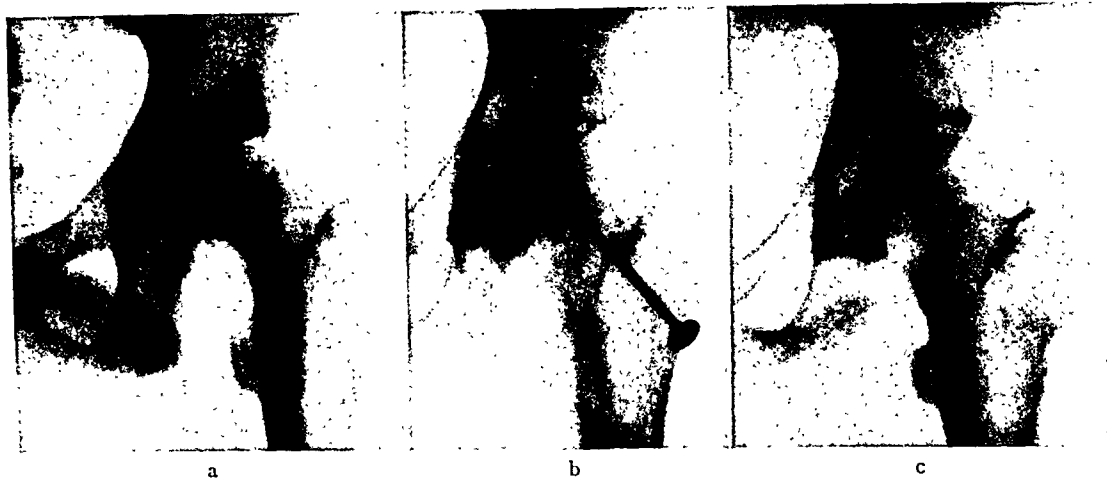


Fig. 3. Male, aged 14 years. a, Symptoms 5 months, sudden increase 3 days previously; callus in inferior angle; head displaced downward  $\frac{3}{4}$  inch, moderately posteriorly; index of motion, 20. b, Three months after open reduction

and nailing; slight overreduction (intentional). c, Roentgenogram of the same hip which was taken 1 year after operation; no pain; view 5 years after operation; index of motion was 66.

limitation of motion (usually abduction and internal rotation) and when there is impingement of the neck against the acetabulum with the resultant tendency to arthritis.

*Treatment in slipping stage.* It is desirable to reduce the deformity when there is one-half inch or more of displacement downward or posteriorly. We have attempted to reduce these deformities when the lesion had not already reached the quiescent stage. It was found in the first study that closed reduction by manipulation into abduction and internal

rotation was unsatisfactory. Partial reduction was obtained in only 3 of 21 cases. These 3 reductions were done shortly after the slip, with no callus in the inferior angle. Only one additional closed reduction has been attempted in the past 10 years, and this resulted in little correction. Most of these hips had some permanent limitation of motion due to the immobilization, and there were occasional circulatory changes in the head, due to tension on the capsule. Better results could probably have been obtained with bed rest alone until

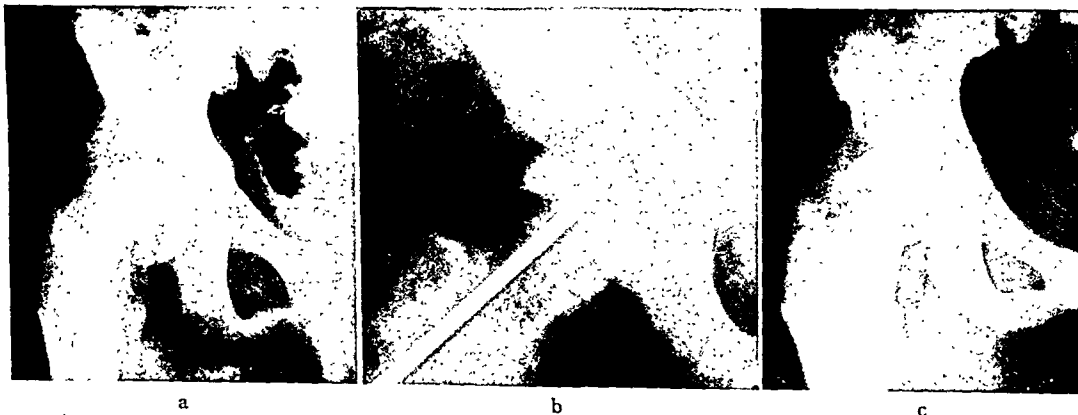


Fig. 4. Male, aged 13 years. a, Symptoms 2 weeks; reduced with Russell traction. Allowed up at 8 weeks and slipped again more than at first. Index of motion, 25. b, Open reduction and nailing. Good reduction. Suspension

and traction for 6 weeks. Nail removed at 7 weeks. Index of motion, 46. c, Two years after operation. Fully active without symptoms; no deformity; index of motion, 90. The best result with open operation.



Fig 5 Female, aged 12 years a, Symptoms 2 months Index of motion, 10, head displaced downward 1 inch, and posteriorly, with neck impinging against acetabulum b, January 3, 1936, open reduction and fixation with Smith-

Petersen nail Motion begun first week, nail removed 8 weeks after operation c, Roentgenogram of same hip which was taken 8 months after operation Index of motion at one year was 36

the condition became quiescent, possibly followed by subtrochanteric osteotomy. This procedure is advised only for recent slips with no callus inferiorly, and nailing might be preferable to plaster immobilization.

**Reduction by strong traction.** Nine years ago we reduced 7 epiphyses by very strong traction followed by internal rotation, and immobilized them in plaster in abduction and internal rotation. The downward displacement was corrected in most of them. Usually the rotation could not be corrected. All of the

epiphyseal discs healed well, but in most of the hips the cortex of the head became irregular, and in some cases irregularly ossified and the joint space thin. Eventual motion was good in only one hip (Fig. 1), fair in one, and poor in the others. This was probably due to injury to the capsule and the circulation by the traction and the tension in plaster. The results would probably have been better had bed rest alone been used until the lesion healed, possibly followed by subtrochanteric osteotomy. Probably nailing such hips after



Fig 6 Male, aged 15 years a, Symptoms 1 year Callus in inferior angle Head displaced downward  $\frac{3}{4}$  inch, moderately posteriorly Index of motion, 90 b, After

open reduction and Lippman screw Fair reduction, c, Thirteen months after open reduction Screw just removed Index of motion, 83



a

b

c

Fig. 7. Male, aged 15 years. a, Symptoms 2 weeks. Preslipping. Index of motion, 90. Pain and spasm. b, Three months after drilling and pegging. c, Five and one-

half years after operation. Patient complains of no symptoms; he is fully active; index of motion, 100. This is an excellent result.

reduction, with early motion instead of plaster fixation would have given better results.

*Open reduction.* Eleven open reductions, 6 of them osteotomies through the proximal end of the neck, were reported in the first series. The operations were done some weeks after the slipping. The results were fair anatomically and functionally. We have done 17 open reductions from January, 1930 to 1939, all through the epiphyseal disc. These are divided into two groups. Eleven of the hips were immobilized in plaster for 10 to 12 weeks. Follow-up ranged from  $2\frac{1}{2}$  to 7 years, averaging  $5\frac{1}{2}$  years. There were only 2 good results, both having had preliminary rest with light traction, one being only 8 years old. The average index of motion was 26 (Fig. 2). Two were complete failures, one later having a fusion operation, the other an arthroplasty. In the second group of 6 hips, internal fixation was used, with active motion from the first week. The follow-up period averaged  $2\frac{1}{2}$  years. The ordinary nail, Smith-Petersen nail, and Lippman screw were each used in 2 cases (Figs. 3 to 6). The results in these 6 cases were far better, 2 being very good, 3 fair, and 1 poor. The average index of motion was

66, the range 36 to 96. There were altogether 5 good results and 9 fair ones among the 28 hips, leaving 14 or 50 per cent poor results. Slight arthritic lipping was usual in the hips followed several years. Internal fixation with early active motion is preferable when open reductions are done. When there is much limitation of motion and spasm, the operation should be preceded by a period of bed rest, preferably with suspension and light traction.

*The drilling operation.* We began to make the diagnosis of the preslipping stage some 10 years ago. It was thought that if the weight of the patient were kept off the hip, slipping would not occur and the lesion would heal. The first such patient was kept in bed several months until the line appeared healed. The epiphysis slipped as soon as she was allowed up. The next patient was allowed to go home to consider admission to the hospital. His epiphysis slipped suddenly on the way home. The preslipping hips have subsequently been treated as emergencies. It was obvious that if weight could be kept off the hip long enough, these lesions would heal. However, it seemed desirable to develop a surer and quicker method. The first operation for producing



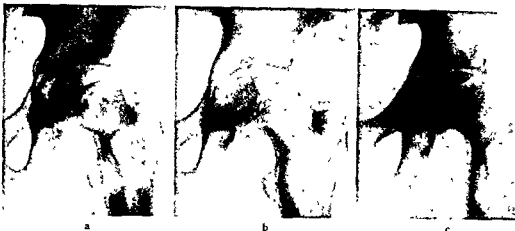


Fig 8. Male, aged 8 years a, Slip  $\frac{1}{4}$  inch, symptoms 3 months Index of motion, 87 Drilled July 31, 1931 No pegs b, Six months after drilling, epiphyseal line healing

c, Eight months after drilling A marked slip after a fall Drilling without pegging does not produce rapid healing and union of the line

premature union and healing of the epiphyseal line was done in December, 1930. The operation has been done upon 17 hips in the preslipping stage, and 23 with slight slips, to January, 1939. The Smith-Petersen approach was used. Several holes were drilled, curetted, or gouged from the neck across the epiphyseal disc into the head, and long thin fragments of bone from the ilium were inserted (Fig 7) Every case has been carefully followed, the average period being  $3\frac{1}{2}$  years. The present report must be considered as preliminary, but the results to date have been very encouraging. There were no deaths or wound infections. There were 3 initial failures in the 40 cases, one preslip and 2 slight slips. One case, among the earliest, had no bone slivers inserted No healing or union occurred and 6 months later the epiphysis slipped badly during a fall (Fig. 8) and an open reduction was done. In the second case, a boy of 11 years, the holes and slivers obviously did not cross the epiphyseal plate (Fig 9). The lesion healed with rest but the epiphysis did not unite and 8 months later the condition recurred. A second successful drilling was then done. In the third case, a girl of 10 years, the lesion healed but the slivers absorbed and union did not occur Eight months later the lesion recurred, and redrilling resulted favorably. Pegs were not used with two other drillings, and in these cases healing and union

were quite slow. In the 35 remaining hips the lesion healed in 8 to 12 weeks and complete bony union across the epiphyseal plate occurred within 6 to 12 months without slipping. It may safely be said that if healing does not occur within these periods the pegs have not crossed the line. The patients were kept recumbent until the lesion healed and spasm subsided. Two of these patients had occasional pain during the follow-up period. Four had a slight residual limp, 4 did not attempt athletics because of obesity, and the remainder denied any symptoms whatever. There was shortening in only one-half of the cases, the greatest being one inch, the average one-sixth inch Since little growth takes place at this epiphysis, the shortening is not enough to be of consequence Internal rotation was slightly limited in 16 hips, flexion in 11, abduction in 9 Limitation of abduction appeared to be due in two of the latter hips to relative overgrowth of the greater trochanter. Arthritic lipping, however slight, was unusual in the longer follow-ups The index of motion ranged from 66 to 100, and averaged 87. Thus the anatomic and functional results were very good or excellent in 39 of the 40 cases, including the two redrillings

It is realized that these results might have been approximated by rest alone with freedom from weight bearing. This may be accomplished by rest in bed, or with a co-op-



Fig. 9. Female, aged 11 years. a, Preslip. Symptoms 3 months. Index of motion, 52. b, Drilled and pegged January 27, 1937. Holes and pegs fail to enter head. c, Eight months after operation. Line not healed or united. Slight posterior slip. d, After second drilling and

pegging. Holes and pegs enter head. e, Ten months after second operation. Line healed and united with no further slip. f, Roentgenogram which was taken 2 years after second operation. Line obliterated, head healthy. Index of motion 80.

erative, intelligent, and fortunate patient, by the use of crutches or a caliper brace. Such treatment would require months or even years in the younger patients. It is to the financial, psychological, physical, and temporal advantage of the patient and those who provide for his care that he be cured as quickly as is reasonably possible. We have not tried nailing these epiphyses because nailing, while it may prevent slipping, does not of itself produce union and it could hardly result in a

quicker or more favorable healing. The drilling operation requires experience in hip surgery and gentleness, for a rough procedure will do more harm than good. The operation is advised under favorable circumstances as the simplest, quickest, and most certain method of curing the disease.

#### SUMMARY AND CONCLUSIONS

The clinical, laboratory, roentgenographic and pathological features of the preslipping

stage of slipping of the upper femoral epiphysis, are described. These features are further discussed in relation to the slipping, quiescent, and residual stages.

The disease is found to be primarily a synovitis occurring during the period of rapid growth. The circulatory disturbance associated with the synovitis results in a softening on the distal side of the epiphyseal plate. The softening is often followed by a gradual or sudden and often progressive slipping of the epiphysis.

The results of the surgical treatment of 103 cases of this condition are reported. These are evaluated in terms of the normal hip and in relation to hips not surgically treated. The importance of rest in the treatment of the acute inflammatory phase of the preslipping or slipping stages is discussed.

Subtrochanteric osteotomy for correction of the deformity is preferred in the quiescent and residual stages.

Closed reduction by abduction and internal rotation has succeeded only in the few cases

manipulated very soon after the first slip. Closed reduction by strong traction and by open operation have been usually anatomically successful. Limitation of motion with secondary circulatory changes in the united femoral head have been the rule in these three groups when the hips were immobilized in plaster after reduction.

Internal fixation with early active motion is preferred after closed or open reduction of the moderately or severely slipped epiphysis.

Hips seen in the preslipping stage or after a slight slip may be treated by rest and freedom from weight bearing but should not be immobilized in plaster. The possibility of recurrence of the lesion in younger children after roentgenographic healing of the disc must be emphasized. An operation for producing early healing and preventing any or further slipping is offered. The results in 40 cases having the operation have been excellent. The importance of early diagnosis and proper treatment before slipping occurs cannot be overestimated.

# CHORIOEPITHELIOMA IN THE MALE

## Treated with Pregnancy Serum

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**I**N this paper we describe a case of chorioepithelioma of the testis treated by us at the Memorial Hospital, and show the results of various hormone tests made on the patient's urine and the effect on the gonadotropic hormone excretion levels produced by the injection of serum from parturient women and cord blood.

In a series of three review articles on the subject of chorioepithelioma in men and women, Mathieu makes repeated mention of the possibility that in the serum of the normal pregnant female there may be substances which are lytic for trophoblastic cells and cell emboli. Schmorl is credited with the observation that careful examination of the lungs of women dying during childbirth revealed that in 80 per cent of the number studied chorionic emboli were present. It has been reasoned that in many respects the growth of the placenta resembles that of a malignant tumor. It is true that chorionic villi invade the uterine musculature in a manner often suggestive of the behavior of a malignant tumor. Bell called attention to this invasive character of the placenta and was of the opinion that if the mechanism of nidation and placentation was thoroughly understood, much light would be thrown on the nature of cancer.

Since emboli from this invasive tissue break off and are carried to the lungs but fail to grow there or to produce metastatic tumors, several authors have suggested that there must be some substance present in the serum of pregnant women and animals which inhibits this growth. Dickson, referring to this possibility, suggests that the logical way to treat chorioepithelioma is by the injection of large quantities of serum from pregnant women or mares. Fortner and Owen believe that the treatment of chorioepithelioma may

eventually be nonsurgical, consisting in serum injections or endocrine therapy. They say that "sera of pregnant animals are now being used but it is too early to expect accurate findings." They mention some work of Fraenkel who "demonstrated that the serum of normal pregnant women is lytic to chorionic epithelium while the serum of women with chorioepithelioma lacks this property." A study of Fraenkel's original paper fails to reveal any such researches. Furthermore, since the Fortner and Owen paper, there has been published, to our knowledge, no report on the progress of the treatment of chorioepithelioma with pregnant serum.

Since 1932, at the Memorial Hospital, 203 cases of tumor of the testicle have been studied by means of the quantitative Aschheim-Zondek test. Of this number 5 were classified by pathological examination as chorioepitheliomas. Of these 5 cases, all but one showed more than 10,000 mouse units per liter of the chorionic gonadotropic hormone. These patients were treated by intensive x-ray therapy in spite of which all quickly succumbed to the rapid progression of the tumor. Contrary to the opinion of some authors, we believe that this type of cancer is very resistant to radiation therapy. Therefore, since the patient, whose case report follows, revealed upon examination widespread metastatic disease, it was decided to follow the suggestions of Mathieu, Dickson, and Fortner and Owen, and give serum from pregnant women, studying carefully at the same time the effect of this treatment on the output of gonadotropic hormone in the urine as well as on the metastatic tumor nodules themselves.

A. L., a 33-year-old white male baker, born in Denmark, while driving his car along the road in January, 1940, noticed a tickling in his throat. On reaching home he examined this area with the aid



Fig. 1. Metastatic chorioepithelioma growing in the right tonsil; the area of tumor growth first discovered by the patient

of a mirror and saw what he thought was a blood clot in the region of his right tonsil (Fig 1). He tried to dislodge this material with a spoon but succeeded only in making the area bleed. A physician was consulted who advised tonsillectomy. This procedure was carried out but the specimen removed was discarded without further examination.



Fig. 3. Marked gynecomastia, accessory nipple beneath the right breast, and a metastasis to the left of the umbilicus.

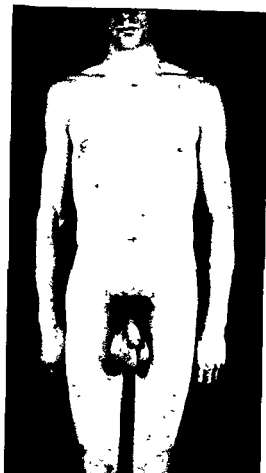


Fig. 2. Full length picture of patient showing testicular primary and metastases on chin and abdomen

A week later a new-growth had appeared at the same site. This time another doctor was consulted who cauterized the area twice. Since 2 weeks later the tumor was still present and growing rapidly, this doctor referred the patient for diagnosis and treatment to one of us (A. H.).

The patient said he had always been well and strong. On close questioning, however, he admitted that for the past month he had felt a little tired and run down. He attached no special significance to this condition.

The complete examination of the patient showed in addition to the tumor of the tonsil, a similar nodule on the chin, a deep subcutaneous bluish nodule 2 centimeter in diameter in the left epigastrium, another nodule about the same size just above the iliac crest on the right, and a fifth one on the medial aspect of the right upper arm. The right testicle contained a hard tumor 6 by 7 by 7 centi-

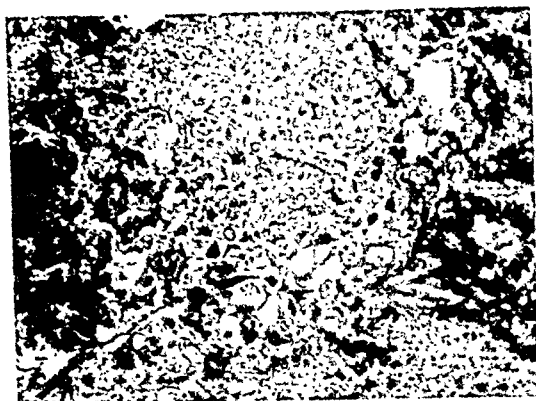


Fig. 4. Microscopic appearance of the tumor, showing syncytial and Langhans cells, hemorrhage, and hyalinizing necrosis.

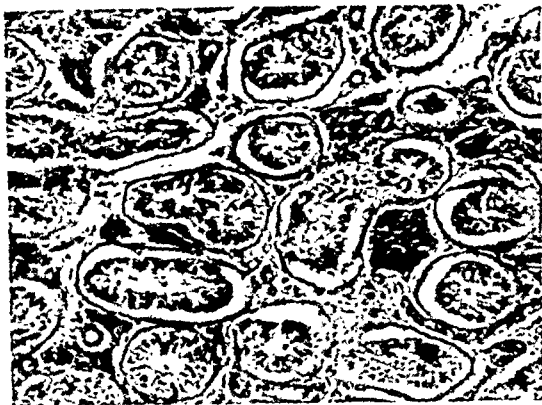


Fig. 5. Interstitial cell hyperplasia in the remaining testicular tissue, with complete failure in spermatogenesis.

meters (Fig. 2) which the patient thought had been present all his life. He had noticed, however, that it had grown slightly during the past 2 years. It had always been painless. He could remember no trauma to it. There was well marked bilateral gynecomastia (Fig. 3), a condition which the patient had first noted 2 weeks previously. Both breasts were slightly sore. The patient was very anemic. X-ray examination of the chest showed extensive bilateral metastases.

In addition to the physical findings already mentioned, a blowing systolic murmur was heard over all the precordium but loudest in the second interspace to the left of the sternum. The blood pressure was 140/60. The liver and spleen were not palpable. The genitalia were not remarkable save for the tumor of the right testicle. The prostate was small. The seminal vesicles seemed somewhat enlarged.

The laboratory findings were: urine, clear; specific gravity, 1020; no albumin or sugar; sediment negative. Blood tests showed hemoglobin, 30 per cent; red blood cells, 2,396,000; white cells, 8,600; polymorphonuclears, 83 per cent; monocytes, 2 per cent; lymphocytes, 15 per cent. There was marked variation in the size and shape of the red cells. The results of the special hormone determinations will be given later.

The patient entered the Hospital on February 2, 1940. He was given transfusions on February 5, 9, 12, and March 1 with 500 cubic centimeters of citrated whole blood on each occasion. From February 5, 1940, to February 26, 1940, he received daily small amounts of deep x-ray therapy. These were directed as follows: upper torso, 25r 8 times to a 50 by 50 centimeter field; lower torso, 25r 8 times to a 50 by 50 centimeter field. The factors were 200 kilovolts; target-skin distance, 150 centimeters; 0.5 millimeter copper filtration. The vertex of the skull was given one treatment of 200r to a 14 by 12 centimeter field, 250 kilovolts, 50 centimeter target-skin distance, 1.5 millimeters copper filtration.

The lesion of the tonsil was treated through a 3 centimeter per oral cone at a target distance of 38 centimeters with 400r, 500r, and 500r at weekly intervals. It did not regress.

The lesion on the chin was implanted with one gold filtered radon seed of 1.82 millicuries. It continued to grow.

The patient rapidly declined and he died on March 9, 1940.

**Autopsy findings.** In addition to the subcutaneous, pharyngeal, and testicular tumors already mentioned, the postmortem examination revealed metastatic deposits in the pleura, lungs, mediastinum, liver, spleen, kidneys and para-aortic nodes, and brain. These were friable and hemorrhagic in appearance. There were several hundred of them in the lungs varying in size from a few millimeters to 3½ centimeters. Most of the metastases in the liver were near the surface in the right lobe. The largest was 2 centimeters in diameter. There were 3 nodules in the spleen, the largest 1.5 centimeters in diameter. Multiple cortical metastases of small size were present in the kidneys. Two nodules were present along the iliac arteries and four similar metastases along the aorta measured 2 to 2.5 centimeters in diameter. In the right occipital lobe of the brain was a 1 centimeter metastatic area, with several smaller metastases deep in the cerebrum. Two metastatic tumors occurred in the cerebellum, the larger 2 centimeters in diameter.

The testicular tumor measured 7½ centimeters in greatest diameter. It was composed largely of typical chorioepithelioma most of which was infarcted, necrotic, and interspersed with extensive areas of hemorrhage (Fig. 4). Parts of the tumor showed cysts lined with columnar mucus secreting epithelium or with stratified squamous epithelium. These structures would seem to indicate the origin of the chorioepithelioma in a complex teratoma of the testis. The remainder of the atrophied testicular tissue formed a narrow rim around the tumor. In

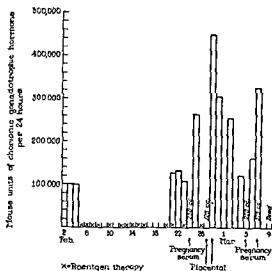


Fig 6 Chart of the urinary excretion rate of chorionic gonadotropic hormone before and after treatment with serum from parturient women and cord blood

this area there was well marked interstitial cell hyperplasia (Fig 5)

A bilateral confluent lobar pneumonia involved all lobes. There were several red, friable, easily detached vegetations on the pulmonary and mitral valves. An incidental finding was a double ureter on the right side.

The pituitary was unusually interesting. It has been reported by Heidrich, Fels and Mathias that histological changes similar to those seen in the pituitary gland of pregnancy occur in the glands of men dying of chorioepithelioma. Stoeckl reported, contrary to this observation, that there was a great increase in deeply granular basophiles. In the present case the pituitary was sectioned and examined by Dr Aura E Severinghaus, who reported as follows:

"The anterior lobe of the hypophysis showed features which are characteristic of the pituitary gland of the pregnant female at full term. The acidophiles were markedly degranulated, and many cell-cords were entirely composed of these cells, which are the so called pregnancy cells. The basophiles were numerous and well granulated. Cytological features which have been associated with increased secretory activity in the cell were prominent in both granular types."

On biological test, the dried gland when ground up and suspended in normal saline failed to cause any changes in the ovaries of immature female rats 21

days old even when given in amounts corresponding to 7 milligrams of dry gland. Normal males, according to Witschi and Riley, have glands which produce vaginal cornification, and ovarian follicular ripening in doses of 1 milligram of dried gland. This decrease in pituitary potency corresponds with the findings in the glands of pregnant women.

**Special hormone determinations and treatment—gonadotropic hormone.** On admission the patient's entire urinary output was collected for 3 days and the number of mouse units of chorionic gonadotropic hormone was determined for each 24 hour output. Before any treatment of any sort had been given these assays showed 40,000, 100,000, and 100,000 mouse units, respectively.

A similar 3 day run was made on February 21, 22, and 23. At this time in spite of 12 treatments with deep roentgen therapy, the total amounts were essentially the same, 125,000, 130,000, and 115,000.

On February 24 the patient was given 250 cubic centimeters of serum intravenously, the serum having been obtained from the blood of two mothers who were in the fourth postpartum day. The result of this procedure, shown in the chart (Fig 6), was characterized by a sharp rise in the gonadotropic hormone to 260,000 mouse units per 24 hours.

On February 27 there was given intravenously 125 cubic centimeters of sterile serum obtained from numerous specimens of placental blood, taken from the cord at the time of delivery. This procedure was followed by a temperature rise to 103 degrees but since the patient did not appear particularly sick another 125 cubic centimeters of serum was given the following day, February 28. The urine specimen collected from 8 00 a m February 28 to 8 00 a m February 29 showed the highest output of gonadotropic hormone recorded for this patient, 440,000 mouse units. The next day, February 29, in spite of continuing high fever the output had dropped to 300,000 mouse units. Two days later, March 2, a day following a transfusion of 500 cubic centimeters of normal citrated blood, the temperature rose to 104 degrees F, while the gonadotropic output fell to 250,000 mouse units. Physical signs at this time suggested bilateral bronchopneumonia. Sulfapyridine was given resulting in a prompt fall in the patient's temperature to 99.2-100.3 degrees. The urinary output of gonadotropic hormone on March 4 was 120,000 mouse units. In brief, then, the injections of 250 cubic centimeters of post partum serum and placental blood serum appear to have raised the urinary gonadotropic hormone excretion from 130,000 mouse units to a maximum of 440,000 mouse units from which point the excretion rate slowly sank to the pre-treatment level. These variations seemed to occur independent of the patient's temperature changes. A similar rise did not follow transfusion with normal male blood.

Two more injections of serum from women 1 to 3 days postpartum were given, the first of 250 cubic centimeters on March 5, and the second of 175 cubic centimeters on March 7. Urinary excretion

of gonadotropic hormone on March 6 had risen to 160,000 mouse units, and on March 7 it was 320,000 mouse units. As the patient's condition became rapidly worse this was the last determination made. He died on March 9 at 7:00 p.m.

From this report we see that there was not only an initial rise in excretion rate after the first sera injections with a return to normal 5 days after their discontinuance, but a second rise following two subsequent injections.

*Estrogenic hormones.* Urine collected for 3 days, February 2 to 5, on the patient's admission, before he had received any therapy was assayed by a modification of the method of Smith and Smith (10) for the three estrogenic hormones, estrone, estriol, and estradiol. The figures obtained from this 72 hour specimen are 53.3 gamma of estrone, 10.7 mouse units<sup>1</sup> of estradiol, and 80 mouse units of estriol. From February 21 to 24 another 72 hour specimen was similarly analyzed and found to contain 111 gamma of estrone, 90 mouse units of estradiol, and 60 mouse units of estriol.

These figures are higher than we have found in the urine of any other male or menopausal female patient we have tested, and they are comparable only with the figures found in the midcycle in menstruating women.

*Androgens.* The same specimens used for the determination of estrogenic excretion rate were also used, after separation into phenolic and neutral fractions, for the determination of the androgens. The colorimetric method of Callow was followed. In the first 72 hour specimen 72 milligrams of "Androsterone equivalent" were found, that is, the color given with the Zimmerman reagent, dinitrobenzene, was equivalent to that produced by 72 milligrams of androsterone. This amount is roughly 24 milligrams a day, a not unusual figure for a normal man. This colorimetric test is specific only for those neutral steroids having a ketonic group in the 17 position and tells nothing about the biological activity of the material.

Consequently we assayed the neutral fraction on the comb growth that could be produced in day-old white leghorn pullets (Dorfman). By this method the neutral fraction was found to contain the equivalent of 3.1 milligrams of androsterone per 24 hours, in its comb stimulating ability. From our experience this is within the range of normal, though perhaps a little lower than the average.

On the second 72 hour specimen collected from February 21 to 24 only the colorimetric type of assay was done. It showed a total "androsterone equivalent" of 17 ketosteroids of 58.8 milligrams or 19.6 milligrams per 24 hours.

<sup>1</sup>Mouse unit=amount necessary to cause full estrus in  $\frac{1}{2}$  of 8 spayed mice injected with the material twice a day for 2 days. The smears were read at 72 hours after the first injection.

*Pregnandiol.* Since in many ways this man's condition was analogous to pregnancy in the female, two assays were made of the product, pregnandiol, shown by Venning and Browne (23) to be the form in which progesterone is excreted in the urine. The amounts of pregnandiol found in the urine during pregnancy are considerable. Bachman, Leckley and Hirschmann report 10 milligrams at the twelfth week of pregnancy to 110 milligrams a week before the onset of labor.

In our patient two 48 hour collections of urine were made, one from February 5 to 7 and the other from February 16 to 18. In each of these an attempt was made to extract sodium pregnandiol glucuronide by the method of Venning and Browne (22). The material so extracted was rather gummy and did not crystallize well at first. It was redissolved repeatedly in alcohol and recrystallized on a steam bath. Finally after washing with petroleum ether, 16.5 milligrams of a clear crystalline substance was obtained from the first specimen and 10.5 milligrams from the second.

Some of these crystals were sent to Dr. Browne who reported that Dr. Venning found them to melt at 210 degrees with the evolution of gas. He said: "the material contains less than 1% of glucuronic acid; it is therefore not a glucuronide. It gave only 1 degree depression of the melting point of pure pregnandiol, so it could probably be free pregnandiol."

If this material was in fact pregnandiol, it would be a finding of considerable interest since such material has not been found in the urine of normal men. It had been thought at one time that pregnandiol was formed only by the action of endometrium on progesterone but this idea has been disproved by the work of Buxton and Westphal who showed that progesterone injected into normal men or men with Addison's disease, may be excreted as pregnandiol. Hamblen, Cuyler and Hirst have confirmed this and have shown, also, that desoxycorticosterone acetate, an adrenal hormone, may also be secreted in this form. Hirschmann found pregnandiol in the urine of ovariectomized women, and Marker found it in the urine of bulls, but not in that of steers. Obviously the precursor of the compound, if progesterone, in these cases, does not come from the corpus luteum, and the logical conclusion is that it is of adrenal origin since it has been established that progesterone is capable of replacing the adrenal cortical hormones in adrenalectomized animals. (Thorn, Engel and Eisenberg, 21; Gaunt, Nelson and Loomis, 9.)



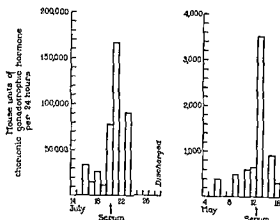


Fig 7 Chart of the urinary excretion of chorionic gonadotrophic hormone in two patients treated with goat serum having a high "antihormone" titre. The goats had been injected over a prolonged period with extracts of pregnancy urine.

#### RÉSUMÉ

Our greatest interest in this case was to discover whether the treatment with the serum of pregnancy would have any effect on the course of the disease or the hormone levels. Obviously such an effect would open possibilities in the treatment of these hopeless types of patients. Previous papers had set forth the logic for such an approach but had given no data. Our expectation was that if any anti-substances were present, these would tend to depress rather than elevate the excretion levels of gonadotrophic hormone. The unexpected rise which this form of therapy brought about can be explained in several ways. It may come from the excretion of the hormone contained in the injected serum, through the patient's urine, though this seems hardly likely. Smith and Smith (18) give values of 25 to 200 rat units of gonadotrophic hormone present per 100 cubic centimeters of serum at the end of pregnancy. A rat unit is usually said to equal 5 mouse units of chorionic gonadotrophic hormone, but allowing for all possible errors it is inconceivable that the administered serum could have contained more than 2 to 4 thousand mouse units while the observed increase in the urine was 300,000 mouse units.

The second possibility is that some specific antiserum is present in the pregnancy serum which either stimulates the tumor cells

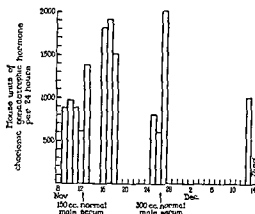


Fig 8 Chart of the urinary excretion rate of chorionic gonadotrophic hormone by a patient receiving injections of normal male serum.

to greater excretion, damages them with a resulting agonal release of hormone, or changes the kidney threshold for hormone excretion. That there may be some specific effect of this kind is also suggested by 2 other cases (Fig 7). Both of these were treated by anti-sera made by injecting goats with pregnancy urine extract until there were present large quantities of antipregnancy "anti hormone." The sera were supplied through the kindness of Dr. A. S. Parkes. In the first case, the serum was rather toxic, giving redness, soreness, and edema at the site of injection. The second serum was not locally toxic. Both gave tremendous rises in the rate of gonadotrophic hormone excretion. In neither case was the patient noticeably benefited, both died ultimately of uncontrolled testicular cancer.

The third and most likely explanation for the rise in excretion rate of gonadotrophic hormone is that it was brought about by some nonspecific protein shock-like reaction following the injection of foreign protein. The pregnant serum was not typed. The cord serum showed very slight amounts of hemolysis, and the patient showed a rise in temperature the day following the serum injection though this was later ascribed to bronchopneumonia.

To test this hypothesis further another patient with teratoma testis has been studied recently in the Hospital (Fig 8). This man had an excretion rate of 880, 960, 880, and 600

mouse units on 4 succeeding days after admission. He was then given 150 cubic centimeters of normal male serum, following which his output rose to 1,360, 1,800, and 1,900. Fourteen days later 300 cubic centimeters of normal male serum was given and his output rose from 800 to 2,000. It sank again to 1,000 the day before his death. The fact that untyped normal male sera intravenously gave a similar though less pronounced effect on gonadotropic hormone excretion in the urine of this patient suggests that nonspecific serum therapy rather than the presence of an antigonadotropic substance caused the changes in gonadotropic hormone excretion rate in the patient with chorioepithelioma.

The normal androgenic excretion rate and the high estrogenic hormone found in the urine explain the gynecomastia, since development of the breast can be brought about in the male by the injection of estrogenic substances. Where the estrogenic hormones come from, whether they arise from the tumor itself or from the adrenals, and what rôle the hypertrophied interstitial cells of the testes play is still unknown. The presence of pregnandiol in the urine suggests abnormally stimulated adrenals though the morphology post mortem was not abnormal. Perhaps the estrogenic hormone also came from the adrenals.

#### SUMMARY

1. Chorioepithelioma of the testis in a man of 33 with autopsy findings is described.

2. The pituitary gland showed both an increase in basophilic cells and the degranulation of the eosinophils characteristic of pregnancy. Biologically, no gonadotropic potency could be demonstrated in the acetone dried gland.

3. The patient excreted in his urine from 40,000 to 130,000 mouse units of chorionic gonadotropic hormone daily. This amount was increased up to 440,000 mouse units by the injection of 250 cubic centimeters of serum from the blood of parturient women and 250 cubic centimeters of serum from cord blood. This increase may have been due to some specific antistubstance in such sera rather than to added chorionic gonadotropic hormone or protein shock. The likelihood is that it was due to nonspecific protein shock.

4. The patient excreted in one 72 hour specimen 533 mouse units of estrone; 10.7 mouse units of estradiol, and 80 mouse units of estriol. In another specimen were 1,110 mouse units of estrone, 90 mouse units of estradiol, and 60 mouse units of estriol. These quantities, which are higher than any found in this laboratory for normal men or menopausal women and comparable, but higher than in normal menstruating women, appear to explain the patient's marked gynecomastia.

5. The androgenic hormone output was normal by colorimetric and biological test.

6. Extraction of two 48 hour specimens of the patient's urine showed 16.5 milligrams and 10.5 milligrams, respectively, of a crystallized hormone thought to be pregnandiol.

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# CARCINOMA OF THE GALL BLADDER AND EXTRAHEPATIC BILE DUCTS

A Clinical and Pathological Study of 117 Cases in 13,330 Necropsies

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**A**LTHOUGH a moderate literature exists concerning carcinoma of the gall bladder and, to a less extent, carcinoma of the extrahepatic bile ducts, a considerable proportion of this material consists of operating room specimens. Clinical correlations with large series of post-mortem examinations are few enough in number to have permitted erroneous conceptions concerning the relative frequency of lesions producing the syndrome of malignant obstructive jaundice, the progression of symptoms, the tendency for metastasis, and the manner of exitus.

In a series of 13,330 consecutive post-mortem examinations performed in the Department of Pathology of the Cook County Hospital between January, 1929, and April, 1940, inclusive, we collected 55 cases of primary carcinoma of the gall bladder and 62 cases of primary carcinoma of the extrahepatic bile ducts. The first 12 cases of our series of carcinomas of the extrahepatic bile ducts were included in a report from this laboratory by Shapiro and Livendahl in 1931. Certain conclusions drawn by these authors bear revision in the light of a more extensive series. One case of melanoblastoma of the gall bladder was previously reported from this laboratory by Rosenthal in 1931.

## INCIDENCE

Of the 13,330 autopsies 1,808, approximately 13.6 per cent, revealed malignant tumors. (For statistical purposes we have included sarcomas and malignant neurogenic tumors with carcinomas.) Fifty-five cases of

carcinoma of the gall bladder constitute 0.41 per cent of all post-mortem examinations and 3.0 per cent of all carcinomas. This compares favorably with the incidence of 0.27 per cent of 11,400 post-mortem examinations reported by Jankelson, and 0.33 per cent of 13,034 autopsies reported by Illingworth. In a recent rather complete statistical review of the literature on carcinoma of the gall bladder Mohardt quotes an incidence of 0.85 per cent among 19,908 necropsies reported by von Berencsy and von Wolff. Among the various authors quoted by Mohardt in establishing the frequency of involvement by cancer of the gall bladder compared to other organs, the values varied from 3 to 13 per cent. In our series the average was 3.0 per cent.

The surgical incidence of carcinoma of the gall bladder is considerably higher than the autopsy incidence and probably less reliable. In a series of papers from the Mayo Clinic the incidence of malignancy decreased from an original report in 1902 of 5 per cent of all diseased gall bladders to a recent figure of 0.5 per cent. Mohardt found an average of 1.12 per cent gall bladders to be malignant in a composite review of over 35,000 operations.

Sixty-two cases of carcinoma of the extrahepatic bile ducts constitute an incidence of 0.46 per cent of all post-mortem examinations and 3.4 per cent of all carcinomas. They were located as follows: in the cystic duct, 7 cases, hepatic ducts, 13 cases, common bile duct, 32 cases, papilla of Vater, 10 cases. Rolleston's 90 cases of carcinoma of the extrahepatic bile ducts were located as follows: in the cystic duct, 6 cases; common hepatic duct, 19 cases, common bile duct, 34 cases; juncture of cystic, hepatic, and common bile ducts, 27 cases, right and left hepatic ducts, 3 cases,

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cystic and common bile ducts, 1 case. Carcinoma of the papilla of Vater is conspicuously absent in this series. In Marshall's series the juncture of the cystic, hepatic, and common bile ducts was the most frequent site; next, the papilla of Vater; and third, the hepatic duct. In McLaughlin's collective review, the common bile duct was the most frequent site whereas the point of confluence of all three ducts was second in frequency; Pallin's statistics are similar with the exception of a higher incidence of involvement of the papilla of Vater. Inasmuch as the point of confluence of the cystic, common hepatic, and common bile ducts is within such close proximity to carcinomas originating in any one of the converging ducts, this area might easily be the most frequent site of secondary extension. In our experience we have been able to localize the tumor to one of the ducts in almost every case.

#### AGE AND SEX

Of the 55 cases of carcinoma of the gall bladder, 21 occurred in males and 34 in females. Of the 55 cases 44 were in the white race and 11 in the negro. Before comparison of our figures for sex and racial incidence can be accurately made with that in the literature, the following fact must be taken into account: that about twice as many autopsies are performed in this institution upon males as upon females, and about twice as many in the white race as in the negro. Therefore, the absolute figures will be as follows: 76.4 per cent of carcinomas of the gall bladder occurred in the female and 23.6 per cent in the male; 66 per cent were of the white race and 34 per cent in the negro. The youngest patient with carcinoma of the gall bladder was 42 years old, and the oldest was 86 years old. The distribution of cases among the age decades was as follows: in the group from 41 to 50 years, 7 cases; 51 to 60 years, 18 cases; 61 to 70 years, 20 cases; 71 to 80 years, 7 cases; 81 to 90 years, 3 cases.

This distribution of cases according to age compares very favorably with a similar classification of 212 cases of carcinoma of the gall bladder recorded by Judd and Gray. The average age varies in different series from 57 to 60 years. Mohardt cites several cases

reported in the literature of carcinoma of the gall bladder in patients 22 and 25 years of age. Mohardt has gathered the results of 9 different contributors who gave figures of from 54 to 100 per cent of all carcinomas of the gall bladder occurring in the female. Perhaps the explanation for this wide range lies in the failure to recognize a disproportion in the incidence of post-mortem examinations between the two sexes. Our corrected figure of 76 per cent appears to coincide with the average.

Forty-four of the 62 cases of carcinoma of the extrahepatic bile ducts occurred in the male and 18 in the female. Of these patients 54 were white, 7 were negroes, and 1 was oriental. The absolute figures for the sex and racial incidence of carcinoma of the extrahepatic bile ducts were 55 per cent in the male and 45 per cent in the female. There were 77.1 per cent in the white race, 20.1 per cent in the negro, and 2.8 per cent in the yellow. Judd and Gray found 58 of 100 cases in the male and in Rolleston's series of 90 cases of bile duct cancer, 55 were in the male. Devic and Gallavardin observed the incidence in their series to be 30 in the male and 16 in the female. Musser's cases were equally divided. The youngest patient was 31 and the oldest 86 years old. The distribution among the age decades was as follows: in the group from 31 to 40 years, 5 cases; 41 to 50 years, 9 cases; 51 to 60 years, 15 cases; 61 to 70 years, 21 cases; 71 to 80 years, 11 cases; 81 to 90 years, 1 case.

The marked predilection of carcinoma of the gall bladder for the female, in sharp contrast to carcinoma of the gastrointestinal tract in general, has been widely appreciated and attributed to the preponderate incidence of cholelithiasis in the female. Although we found that carcinoma of the extrahepatic bile ducts showed a definite tendency to occur at an earlier age than carcinoma of the gall bladder, yet the occurrence of the majority of the cases was in the sixth and seventh decades. This is in complete agreement with other investigators.

#### CLINICAL PICTURE IN CARCINOMA OF THE GALL BLADDER

In no clinical entity is a closer relationship between symptomatology and pathology more



Fig 1 (P.M. 478-40) Clinically silent carcinoma of the papilla of Vater. Note metastases to the regional lymph nodes and liver. Patient died of peritonitis following a recurrent perforation of a posterior duodenal ulcer.

evident than in carcinoma of the biliary structures. For this reason we find it difficult to group the symptoms found into definite symptom-complexes such as has been done by Lancereaux and by Rolleston. We prefer to report our findings upon a statistical basis, bearing in mind all the while that each clinical history is entirely dependent upon the sequence of pathological events within the porta hepatis, based upon pre-existing pathological changes as well as upon those in the making.

In 34 of our 55 cases, 61.8 per cent, there were complaints of pain at some time during the clinical course; pain was most frequently referred to the right upper quadrant, less frequently to the epigastrium, and least frequently to the right lower quadrant. The severity of pain was seldom such that demanded morphine for relief; it was usually described as a chronic recurrent type of dull pain. In 16 of the series a definite history suggestive of previous gall-bladder disease could be established. Five patients who complained of pain during the clinical course were found at autopsy not to have either cholecystitis or cholelithiasis. On the other hand, there were 13 cases of cholelithiasis, with or

without cholecystitis, in which the patient did not experience pain. It has been our experience at the Cook County Hospital that although 9 per cent of all post-mortem examinations reveal gall stones, 88 per cent of the cases were without symptoms. Therefore, we must include some other factor in addition to cholelithiasis for the explanation of pain in carcinoma of the gall bladder. With an incidence of pain in over 60 per cent, we cannot agree with Upcott who lists as the most striking clinical features of cancer of the gall bladder, the absence of pain, intense jaundice, and extreme emaciation.

Jaundice occurred at some time in the clinical course of 34, or 61.8 per cent of the 55 patients. In the majority of cases it was present at the time of admission, was persistent and progressive, and associated with clay-colored stools in 12 cases. Of the 34 cases 14 were associated with pain and 11 without pain; on the other hand, 20 cases of the series of 55 in which pain was a factor were not associated with jaundice. Seven patients of the 55 developed jaundice as a terminal condition and are therefore not included among the 34 with symptomatic jaundice. The icterus index

levels were constantly elevated in all cases of jaundice, ranging from 65 to 250, but usually less than 100. The van den Bergh test, when made, gave a direct immediate reaction.

Gastrointestinal symptoms were listed in 30 of the 55 patients and usually consisted of a vague dyspepsia, anorexia, nausea, and occasional vomiting. Although these symptoms frequently led to the suspicion of carcinoma of the stomach, their relative mildness together with the usual presence of the characteristic pain, with or without jaundice, militated against such a diagnosis. Diarrhea, constipation, and melena were rather infrequent complaints. Judd and Baumgartner divided the cases of gall-bladder carcinoma as follows: a group comprising 70 per cent of the cases which presented history of biliary colic and dyspepsia dating back many years and then a sudden appearance of jaundice, dull pain, and a palpable tumor; a second group of 22 per cent listed complaints compatible with chronic cholecystitis alone; the remaining 8 per cent presented themselves in a terminal state with evidences of cachexia, carcinomatosis, jaundice, and ascites. On account of the nature of our institution, a much larger proportion of our patients constitutes this latter group.

Thirty-one of the 55 cases were admitted in a state of cachexia; this might be anticipated in a large municipal charity institution. Weight loss was sometimes extreme, as much as 60 pounds in 6 months but usually in the vicinity of 20 pounds during the course of the illness. In 12 of these 31 cases the patient complained of a palpable mass. The duration of illness was usually between 3 and 6 months, the shortest being 1 month and the longest 3 years; only 9 of the 55 patients lived more than 6 months after the initial complaint. Judd and Gray found that in most of their 212 cases of carcinoma of the gall bladder, the duration of illness was less than 6 months, and that in one-half of these symptoms had persisted for 2 months or less. Twenty-two of the 55 patients presented complaints of dependent edema and ascites, the ascites frequently requiring abdominal paracentesis.

On physical examination, 35, or 63.3 per cent, of 55 patients presented a palpable liver;

13 presented a palpable gall bladder, and 4 others presented a palpable extrahepatic mass. In only 2 instances was the gall bladder alone palpable. The presence of a palpable gall bladder in only 23.6 per cent of these cases places considerable doubt on the value of this finding, despite its frequent emphasis by earlier writers. Twenty-one, or 38 per cent, of these cases proved to have a fluid wave suggestive of ascites.

In 20, or 36.3 per cent, a profound secondary anemia was found, 7 cases showed blood in the stool, and in another 7 cases no free acid was shown on gastric analyses. The gall bladder failed to concentrate x-ray opaque dyes in 10 instances and x-ray opaque stones were visualized in 2 cases. The nonprotein nitrogen and creatinine were frequently elevated depending upon the intensity of the jaundice, but an albuminuria was very common. Cholesterol levels of the blood were determined in only 4 patients, but in all of these it was much higher than normal. It became apparent that laboratory aids in the diagnosis of carcinoma of the gall bladder are of only slight help. However, our series of cases show a greater tendency for secondary anemia than is ordinarily believed to be present in this neoplasm.

#### CLINICALLY SILENT CARCINOMA OF THE GALL BLADDER

We wish to draw special attention to 4 cases of carcinoma of the gall bladder which we believe were clinically "silent." At least they presented no symptoms or physical findings which could warrant a diagnosis, and we mention them to illustrate the insidious nature of the disease. A 60 year old colored female was believed to have peritonitis, of which she died a few days after admission; however, the cause of the peritonitis was found at autopsy to be due to a spontaneous ulceration of the gall bladder into the colon, the fundus of the gall bladder containing a polypoid adenocarcinoma without evidence of metastasis. Another 60 year old colored female died of peritonitis due to a traumatic rupture of the rectum, but in addition a scirrhous adenocarcinoma of the fundus of the gall bladder was found which had extended

into the liver bed. A 48 year old colored male was believed to have a central nervous system syphilis, but on post-mortem examination these symptoms proved to be due to a melanoblastoma of the neck of the gall bladder which had metastasized to the brain, as well as elsewhere. A 59 year old white female presented the classical symptoms and signs of pernicious anemia with cord degeneration, of which she died. At autopsy she presented a papillary adenocarcinoma of the gall bladder which had metastasized to the liver and produced a spontaneous cholecystoduodenostomy.

#### CARCINOMA OF THE EXTRAHEPATIC BILE DUCTS

Pain was present in 26, or 41.9 per cent, of 62 cases. The pain was usually of dull character, most frequently localized in the mid-epigastrium and less frequently to either right quadrant of the abdomen. Fourteen of the 26 patients complaining of pain were without evidence of cholecystitis or cholelithiasis; on the other hand, 6 cases of cholelithiasis and 2 of cholecystitis did not list pain as a symptom. Eleven of the 62 patients gave a definite history of previous gall-bladder colic. The fact that a source other than the gall bladder must be looked for as the explanation of pain becomes even more apparent in carcinoma of the extrahepatic bile ducts than in carcinoma of the gall bladder. Musser has demonstrated the invasion of the nerve bundles of hepatic ducts by the neoplastic cells and offers that for the explanation of pain. Of a series of 20 patients with carcinoma of the bile ducts reported by Renshaw 12 experienced pain varying from a dull ache to severe biliary colic; 11 of his patients gave a history of cholecystitis or cholelithiasis for an average length of time of 5 years.

Of the 62 patients with bile duct cancer 57, or approximately 92 per cent, presented jaundice as a dominant symptom sometime during the clinical course, the majority of these patients noting this complaint early in course of the illness. Jaundice is still recognized as the most reliable symptom, for above all other symptoms it focuses attention directly upon the porta hepatis. The 5 remaining cases

which did not list jaundice as a symptom constitute a group of cases to which we shall refer to shortly as clinically "silent" lesions of the extrahepatic bile ducts. In 26 of the 57 jaundiced patients, pain of a type described was also present. The jaundice was associated with acholic stools in 29 instances and with the complaint of biliary in 5. Pruritis is a frequent accompaniment. The jaundice is almost invariably unremitting once established, but early in the clinical course the jaundice may be transient. This type is supposedly due to temporary edema or spasm of the common duct which is spontaneously relieved. Shapiro and Livvendahl mention the ulceration of an obstructing neoplasm of the common duct as the mechanism of temporary resumption of bile flow late in the disease. We have seen 3 cases of carcinoma in the vicinity of the ampulla of Vater which have become necrotic and ulcerated into the duodenum; however, in none of these was there relief from the obstruction to bile flow. Therefore, we cannot see any value in utilizing this as a differential point between carcinoma of the papilla of Vater and carcinoma of the head of the pancreas.

Here, as in carcinoma of the gall bladder, the frequency of mild complaints referable to the gastrointestinal tract, is surprisingly high. In 32 of the 62 patients there was nausea, anorexia, and vague dyspepsia. Constipation was more common than diarrhea. Complaints of postprandial pain relieved by soda or food was not altogether uncommon. Five patients of the series of bile duct cancer were found to have chronic duodenal ulcers and in 1 instance a severe duodenitis. This is of particular interest in that the malignant transformation of a duodenal ulcer has been suggested as a possible pathogenetic agent in carcinoma of the common bile duct and papilla of Vater, just as is gastric carcinoma.

Of the 62 patients with bile duct carcinoma 34 patients showed evidences of cachexia and weight loss, frequently extreme. Four patients complained of palpable masses on admission. The average duration of the illness is definitely shorter than for carcinoma of the gall bladder. We found that in most cases it varied between 2 and 4 months, only 1 pa-

tient surviving after 1 year. Probably this fact is to be explained by an earlier cholemia rather than a more malignant neoplasm.

In 30 of the 62 cases dependent edema and ascites suggested portal obstruction in the differential diagnosis.

In view of former teaching, tabulation of physical findings is rather disappointing. In 37 of the 62 cases the liver was palpable and in only 19 was the gall bladder palpable; this gives a percentage of palpable gall bladders on clinical examination of approximately 30 per cent. In a series of 20 cases of bile duct cancer reported by Renshaw, only 6 had palpable gall bladders. Courvoisier's law is verified to a much greater extent by laparotomy and autopsy than by bedside examination. Other palpable metastatic extrahepatic masses were noted in 4 cases.

A profound secondary anemia was observed in 19 of the 62 cases. A markedly elevated icterus index was characteristic, frequently in the neighborhood of 100 units; repeated determinations showed a tendency to rise rather than decrease just prior to death. Biliuria was consistent and usually marked. Chemical blood was observed in the stools of 35 of the 62 patients, an observation that has received little emphasis. Melena is no more characteristic of carcinoma of one area of the extrahepatic biliary system than of another. Gastric analyses revealed an achlorhydria in 8 of 62 cases. In 13 of the patients there was a failure of the gall bladder to visualize and in 2 gall stones were seen. In 4 the non-protein nitrogen rose slightly above 40 milligrams per cent, but in all other cases it was within normal range as was the creatinine. Albuminuria appears to be a frequent accompaniment of icterus. Blood cholesterol was determined in only 5 cases and showed marked elevations in all instances. While van den Bergh tests were not made routinely, when performed they showed a direct immediate reaction.

That the diagnosis of primary carcinoma of the gall bladder or extrahepatic bile ducts is difficult is not to be disputed. The most difficult concept to alter is that carcinoma of the head of the pancreas is the most frequent cause of progressive jaundice which is asso-

ciated with a distended gall bladder and generalized cachexia. It has been our experience that both carcinoma of the extrahepatic bile ducts and carcinoma of the gall bladder occur more frequently than carcinoma of the head of the pancreas (41 cases) as a cause of obstruction of the biliary tract. Moreover, we have found pain to be associated with the jaundice in all 3 of these malignancies far more often than heretofore acknowledged. Clinical diagnosis in 55 cases of carcinoma of the gall bladder included: primary carcinoma of the gall bladder, 12 cases; carcinoma of the extrahepatic bile ducts, 3 cases; carcinoma of the head of the pancreas, 2 cases; carcinoma of the gastrointestinal tract, 16 cases; carcinoma of the liver, 5 cases; cholecystitis and cholelithiasis, 4 cases; peritonitis, 1 case; carcinoma without known primary site, 2 cases; miscellaneous (including "silent" cases) 6 cases; no diagnosis, 4 cases.

The diagnosis was correct in 21.8 per cent of the cases. The clinical diagnosis in 62 cases of carcinoma of the extrahepatic bile ducts included: carcinoma of the head of the pancreas, 20 cases; carcinoma of the gastrointestinal tract, 12 cases; carcinoma of the extrahepatic bile ducts, 13 cases; carcinoma of the gall bladder, 3 cases; portal cirrhosis, 4 cases; primary carcinoma of the liver, 2 cases; cholecystitis and cholelithiasis, 3 cases; obstructive jaundice (cause unknown), 3 cases; peritonitis, 1 case; perforated peptic ulcer, 1 case. The diagnosis was correct in 20.9 per cent of the cases.

Rolleston states that in not one of 48 cases of carcinoma of the gall bladder reported from Guy's Hospital was a correct diagnosis made. Similarly, Boyce and McFetridge report only 2 cases in 25 in which a correct diagnosis was made before operation and 4 cases of carcinoma of the gall bladder in which it was suspected. Only 2 cases in Jankelson's series of 48 gall-bladder carcinomas were diagnosed correctly. In view of the fact that the 3 cardinal findings, viz., pain, jaundice, and a palpable tumor, are not always associated in one case, diagnostic errors appear quite understandable.

We would like to describe in some detail those cases to which we have already alluded



as "silent" carcinomas of the extrahepatic bile ducts. The popular concept of a neoplasm of the biliary tract is that occlusion occurs early in its course and subsequently is followed by icterus. In 5 cases the neoplasm was an incidental finding at necropsy and was not directly contributory to the cause of death.

#### CLINICALLY SILENT CARCINOMA OF THE EXTRAHEPATIC BILE DUCTS

**CASE 1.** A colored male of 67 years entered the hospital with symptoms of dull epigastric pain, nausea, anorexia, vomiting, ascites, and dependent edema; within 1 week the patient died of an acute fibrinous peritonitis, and at autopsy an infiltrating adenocarcinoma of the cystic duct with metastases was found. The gall bladder was shrunken and the liver of normal size.

**CASE 2.** A white female 76 years of age presented symptoms suggesting carcinoma of the stomach and organic heart disease, the patient died of bronchopneumonia after a month's stay in the hospital, and the post-mortem examination revealed an infiltrating adenocarcinoma of the common bile duct which had extended to the liver and pancreas without producing obstruction of the duct itself.

**CASE 3.** A white male 61 years of age entered the hospital with a history suggestive of alcoholic cirrhosis of the liver, the patient died following a massive hematemesis. At necropsy a ruptured esophageal varix associated with an atrophic cirrhosis of the liver in addition to a papillary adenocarcinoma of the common bile duct was found notwithstanding the fact that there was a congenital absence of the gall bladder and cystic duct.

**CASE 4.** A white female 40 years of age died of peritonitis following subtotal gastrectomy for recurrent perforation of a posterior duodenal ulcer, at autopsy a medullary adenocarcinoma of the papilla of Vater with metastases to the peribiliary, peripancratic, and periesophageal lymph nodes was found (Fig. 1).

**CASE 5.** A colored male 35 years of age entered the hospital with symptoms of intestinal obstruction which abated with conservative treatment. It was later thought that a tuberculous peritonitis was present and on autopsy an infiltrating adenocarcinoma of the cystic duct with generalized metastases was found which had not encroached upon any of the other biliary structures.

#### PATHOLOGY

Carcinoma of the gall bladder and carcinoma of the extrahepatic bile ducts have essentially the same pathological types and our description shall apply to both. We have included 7 cases of sarcoma along with these

to facilitate discussion, for other than its histological differences it deserves no separate mention. We have classified the various histological types in Table I.

TABLE I.—CLASSIFICATION OF HISTOLOGICAL TYPES OF CARCINOMAS STUDIED

	No. cases	Total
<b>Gall bladder</b>		
Infiltrating adenocarcinoma	27	
Papillary adenocarcinoma	14	
Mucus producing adenocarcinoma	3	
Medullary carcinoma	8	
Sarcoma	2	
Melanoblastoma	1	
Total cases of carcinoma of gall bladder	55	55
<b>Extrahepatic bile ducts</b>		
Cystic duct		
Infiltrating adenocarcinoma	6	
Medullary carcinoma	1	7
Common hepatic duct		
Infiltrating adenocarcinoma	10	
Papillary adenocarcinoma	3	13
Common bile duct		
Infiltrating adenocarcinoma	24	
Papillary adenocarcinoma	5	
Medullary carcinoma	3	32
<b>Papilla of Vater</b>		
Papillary adenocarcinoma	7	
Infiltrating adenocarcinoma	2	
Squamous cell carcinoma	1	10
Total cases of carcinoma of extrahepatic ducts		62

Papillary adenocarcinoma is thought to originate from benign papillomas of the mucosa either of the gall bladder or the duct involved; the relative frequency with which benign papillomas of the gall bladder are encountered in surgically removed gall bladders is 10 per cent according to Judd and Baumgartner. The papillary adenocarcinoma is a fungating mass which projects into the lumen, in the bile ducts it is frequently pedunculated. On histological examination, the tumor cells cover a central stalk of connective tissue. This type of carcinoma may replace the gall bladder from within and is apt to produce an empyema of the gall bladder by direct extension of the polypoid tumor into the cystic duct, however, we have seen empyemas of the gall bladder associated as frequently with infiltrating and scirrhous adenocarcinomas as with papillary adenocarcinoma. The latter does tend to undergo more rapid necrosis and therefore pre-

disposes to infection of the gall bladder. This type of tumor is less invasive and less malignant and should permit a longer life span although our records of the duration of illness show no significant difference to justify this conclusion; similarly, our statistics on the frequency of metastasis show no lessening of that tendency in this type of tumor.

The infiltrating adenocarcinoma appears to be by far the most frequent type of tumor encountered. It is composed of atypical alveoli of tumor cells which invade all the layers of the gall bladder or biliary duct and convert it into a rather rigid, contracted organ. In the biliary tract this type of tumor takes the appearance of an ulcerated thickened plaque overlying and replacing the mucous membrane. This tumor is prone to produce a shrunken gall bladder or a stenotic duct. As the histological term of this tumor suggests, it tends to invade adjacent structures early and produce widespread metastases. It is considered far more malignant than the papillary adenocarcinoma. The degree of fibrous tissue reaction varies.

Next to the stomach, the gall bladder is supposed to be the most frequent site for the production of mucus-producing carcinomas. It is a degenerative change expressive of an overactivity of the mucus-producing activity of the glands of the gall-bladder mucosa. This is the type of tumor most apt to cause a spontaneous perforation of the gall bladder into a neighboring viscus; however, none of our examples of this complication occurred in this type of carcinoma. Perforation of the gall bladder was seen as frequently with papillary as with infiltrating or scirrhous adenocarcinomas. All 3 cases of mucus-producing adenocarcinoma occurred in the gall bladder and none was found among the biliary tract neoplasms. All 3 cases showed metastases. Although this type of tumor occasionally gives rise to a Krukenberg tumor of the ovary, none of our patients developed metastasis to the ovary.

Although medullary carcinoma is better used as a term of gross description, we imply a tumor that has a solid grayish-white appearance not unlike the white matter of the cerebral cortex which on histological examina-

tion is composed entirely of closely packed alveoli filled with tumor cells with little intervening stroma. Of 6 such cases, 3 occurred in the gall bladder and 3 in the extrahepatic bile ducts. The tumor is quite malignant and shows widespread metastasis.

Squamous cell carcinoma most likely originates from metaplastic mucosal epithelium which is probably a response to chronic inflammatory change. This at least is comparable to the formation of squamous cell carcinomas in other organs normally lined by cylindrical epithelium. Clinical reports of squamous cell carcinoma of the gall bladder exist in fair number, but few of these are described in the bile ducts. Our only case of this type involved the papilla of Vater, the tumor ulcerating into the duodenum and metastasizing to the regional lymph nodes and the liver. The clinical picture in this case was a classical one of malignant biliary obstruction. Fehr and Cabot have reported similar cases.

Although sarcoma of the gall bladder is reputedly rare, we have 2 cases in our series of 55, previously reported by Ragins. Neither of these 2 tumors produced jaundice, and the patient died of the metastasis rather than of the usual cholemia. Rolleston gathered 19 cases of sarcoma of the gall bladder from the literature. The most recent case report is that of Erdmann.

Among the more rare tumors we found in the gall bladder was a melanoblastoma in a 37 year old colored male to which we have already referred. A primary melanoma of the ampulla of Vater is described by Duval.

The obstruction to bile flow can be accomplished by one of three mechanisms or a combination of them: (1) annular stricture of the rigid carcinomatous duct; (2) plugging of the lumen by a projecting polypoid mass; and (3) pressure of enlarged metastatic peribiliary lymph nodes. According to Vander Veer and to Wahl, the low pressure of the bile and spasm of the smooth muscle structures within the biliary tract are additional factors favoring obstruction. To this might be added inflammatory changes due to stones, and edema of the mucosa which are frequently found to be associated with the neoplasm.

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The fate of the liver in carcinoma of the gall bladder or bile ducts may result in: (1) an obstructive biliary cirrhosis; (2) an ascending cholangitis; (3) liver abscess; and (4) metastases. In biliary cirrhosis the liver is usually enlarged, exceedingly firm, has a dark green hue, and on section the marked dilatation of the extrahepatic bile ducts is prominent. The histological picture is one of marked imbibition of bile pigment by the parenchyma, bile casts in the dilated biliary capillaries, and a marked proliferation of fibrous tissue, and lymphocytes within the portal triads. Occasionally a zonal necrosis of the liver lobule is noted. Cholangitis tends to produce a much softer liver which on section will leave upon the cut surface. On histological examination the thickening of the portal triads is found to be due not only to increased fibrous tissue but to an acute inflammatory exudate which consists of polymorphonuclear leucocytes and pus cells which tend to surround the proliferating distended bile ducts. Although the sinusoids contain large numbers of leucocytes the liver parenchyma is uninvaded unless the cholangitis has progressed to the point of abscess formation. The liver abscesses usually tend to be small; they are scattered everywhere throughout the parenchyma and are filled with a light green, purulent material. The abscesses produce local necrosis with compression atrophy of the adjoining parenchyma.

A central zone of necrosis of the liver lobule due to the stasis of bile and a resultant reversal in direction of the flow of bile occur, according to Fuetterer, Herring and Simpson produced a similar result in experimental obstruction of the bile duct.

In carcinoma of the gall bladder, evidence of an obstructive biliary cirrhosis was seen in 26 cases; it is frequently difficult to tell how much of the liver enlargement is due to the cirrhosis and how much to the metastases for the liver was the site of metastasis in 35 of 55 cases. Obstructive cirrhosis is more common in carcinoma of the extrahepatic bile ducts. We found biliary cirrhosis in 51 of 62 cases of bile duct cancer, although the liver was the site of metastasis in an identical number, it does not necessarily imply that the two processes were always coexistent.

There were 7 instances of cholangitis in the cases of carcinoma of the gall bladder and 3 in carcinoma of the extrahepatic bile ducts; the difference can be correlated with the greater frequency of empyema of the gall bladder in cases of carcinoma of the gall bladder. There were 3 cases of liver abscess in 55 cases of gall-bladder carcinoma and 2 cases of liver abscess in the 62 cases of bile duct carcinoma.

Of 55 cases of carcinoma of the gall bladder, 20, or 36.3 per cent, gave evidence of cholecystitis and 40, or 72.6 per cent, gave evidence of cholelithiasis. In 8 of the 40 cases, stones were found in the bile ducts as well. In the series of cases from 24 different authors cited by Mohardt, the incidence of calculous carcinomatous gall bladders varied from a low of 64.6 per cent to a high of 100 per cent. In our own series of 13,300 consecutive autopsies, the post-mortem incidence of gallstones was 9 per cent, 88 per cent of these being without clinical history referable to the gall bladder. The incidence of calculous gall bladders which develop carcinoma is 3 per cent in our series. Among 17 contributors listed by Mohardt, this figure ran from 1.14 to 15 per cent, the average being 4 to 5 per cent. It has been our experience that 6 per cent of all men past 50 and 14 per cent of all women past 50 possess gall stones at autopsy.

Of 62 cases of carcinoma of the extrahepatic bile ducts, 14, or 22.5 per cent, gave evidence of cholecystitis and 19, or 30.6 per cent, gave evidence of cholelithiasis. Three of the 19 cases contained stones within the common duct. Gallstones were present in about one-third of the cases of Rolleston's series of bile duct carcinomas. In each of McGlinn's 5 cases of bile duct cancer, out of 9,000 post-mortem examinations gallstones were present. The incidence of common duct stones is usually placed at 15 per cent of all cases of cholelithiasis. Mayo-Robson considers gallstones a greater factor in the etiology of cancer of the bile ducts than is generally accepted. Of our 41 cases of carcinoma of the head of the pancreas 8, 14.5 per cent, showed cholecystitis and 4, 9 per cent, showed cholelithiasis. Most authors have accepted the rôle of cholelithiasis in the etiology of carcinoma of

the gall bladder as certain. The reasons for this have been chiefly two: First is the frequent association of carcinoma of the gall bladder and stones, of which our figures are quite representative. That stones should cause cancer has been explained by the possibility that the chronic irritation they induce might predispose to cancer, that the stones possessed some radioactive substance (Lazarus-Barlow), and finally that the stones might contain some carcinogenic agent. The second piece of evidence is the experimental production of cancer of the gall bladder in guinea pigs by the introduction of gall stones and foreign bodies. This work had long been accepted and confirmed until investigators, such as Burrows, pointed out that though a stone might produce a cystic hyperplasia of the mucosa of the gall bladder, this was a far cry from cancer itself.

The fact that the disease normally has an incidence of only 14 per cent gall stones in the sex and age group which it most frequently attacks, together with the fact that in a closely related disease—carcinoma of the extrahepatic bile ducts—the incidence of stones is 30.6 per cent, which few will accept as the etiological factor in that disease, should deter us somewhat from overemphasizing cholelithiasis as the sole possible etiological agent. Ewing suggests a combination of multiple factors including the irritative effect of calculi, cellular hyperplasia following inflammation, high cholesterol concentration within the gall bladder, and the irritative effect of bile.

To complete the discussion on the etiology of neoplasm as far as the extrahepatic bile ducts themselves are concerned, some interesting suggestions first made by Rolleston should be mentioned. He suggested the malignant transformation of an ulcer of the biliary tract mucosa, such as occurs in a small percentage of peptic ulcers, as the mechanism in the origin of bile duct cancers. Two case reports by MacCarty emphasize this possibility. Both of these duodenal ulcers involved the papilla of Vater and produced a clinical picture of obstructive gall-bladder disease rather than peptic ulcer.

We have already stated that Courvoisier's law is verified more often by post-mortem studies than by clinical experiences. In the

55 cases of carcinoma of the gall bladder, the gall bladder was found to be distended in 16 cases, and in the group of carcinomas of extrahepatic bile ducts, distention of the bile ducts was noted 18 times. Doubtless dilatation of the gall bladder occurs most frequently when the neck of the gall bladder is involved, and dilatation of the bile ducts is probably a compensatory action rather than an obstructive phenomena. In 10 cases the gall bladder was markedly shrunken and only 1 of them was infected. The shrunken gall bladders were always seen associated with infiltrating or scirrhus carcinomas. Hydrops of the gall bladder was seen in 5 cases, in 2 of these the clear mucinous fluid filled a gall bladder of normal size. Eleven cases of empyema of the gall bladder were found, 6 associated with marked distention of the gall bladder. In all but 2 of the 11 cases of empyema, stones were present, and in all 5 cases of hydrops stones were present.

In carcinoma of the extrahepatic bile ducts the gall bladder was distended in 39, or 62.9 per cent, and there was a distention of the bile ducts above the site of obstruction in 48, or 77.2 per cent, of the cases. Musser lists dilatation of the ducts in 9 of his 18 cases of cancer of that structure, whereas Devic and Gallavardin described 7 distended gall bladders in 14 cases of cancer of the cystic, hepatic, and common bile ducts. Courvoisier stated that dilatation of the gall bladder occurs in 84 per cent of all cases of cancer involving the bile ducts. It has been our experience and that of others that this figure is too high and that actually it lies between 50 and 60 per cent. There were 6 instances of hydrops of the gall bladder, in only 3 were stones present, and in 2 the gall bladder was not significantly enlarged. There were 4 cases of empyema of the gall bladder in this series and all of them were associated with stones and distention of the gall bladder.

Other complications of carcinoma of the biliary tract not already mentioned include perforation, pericholecystic abscess, and biliary peritonitis. In 55 cases of carcinoma of the gall bladder there were 3 perforations into the peritoneal cavity, 5 into the colon, and 3 into the duodenum. In 3 of these 11 cases, per-

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foration was followed by a fatal biliary peritonitis. Spontaneous perforation of a carcinomatous gall bladder occurred in 10 of Musser's 100 cases and in 6 of Reidel's 77 cases. Boyce reports 2 cases of perforation into the peritoneal cavity in 25 cases of carcinoma of the gall bladder. Four cases of pericholecystic abscess were seen, and usually the extension was directly into the liver bed. There was 1 case of liver abscess and 1 subphrenic abscess, both of which ruptured into the peritoneal cavity and led to a fatal purulent peritonitis. Biliary peritonitis followed cholecystostomy in 1 instance whereas 1 case of biliary peritonitis was seen to develop without any apparent mechanical leak.

In 62 cases of carcinoma of the extrahepatic bile ducts there were 4 cases of biliary peritonitis, all without evidences of a mechanical leak; these were attributed to a transudation of gall bladder contents through its distended edematous wall. Three other cases of biliary peritonitis followed surgical procedures. One case of fibrinous peritonitis followed subtotal gastrectomy for a perforating ulcer, and another case was apparently hematogenous in origin. In 1 case a large pericholecystic abscess ruptured and produced a purulent peritonitis.

Ascites was a frequent finding. This is attributed to the following carcinomatosis of the peritoneum and mesentery, obstruction to the portal vein by pressure of metastatic lymph nodes or intrahepatic tumor masses, and cirrhosis of the liver.

The effect of the carcinoma of the biliary tract upon the pancreas is not often mentioned. Although experimental mechanical occlusion of the pancreatic duct is supposed to produce an acute necrosis of the pancreas, no instance of this was found in our entire series, although the pancreatic duct was often occluded to the extent of producing a marked dilatation of the duct of Wirsung. This occurred in 3 cases of gall bladder carcinoma and 11 cases of extrahepatic bile duct carcinoma. The changes found in the pancreas were as follows: In carcinoma of the gall bladder, 2 cases showed an atrophic fibrosis of the pancreas, 2 showed some fat necrosis, and 1 showed an extensive lipomatosis, while in

carcinoma of the biliary tract, there were 10 cases of an atrophic fibrosis, and in 5 some degree of fat necrosis. Disturbed pancreatic function was not observed.

Another frequently overlooked factor in the syndrome of obstructive jaundice is the effect of the cholemia on the kidneys. Changes occur in the renal tubules such as deposits of bile in the tubular epithelium and formation of bile casts. This condition is known as "icteric nephrosis" (a form of tubular nephrosis). Albuminuria and nitrogenous retention are frequently observed clinically. Among the gall-bladder carcinomas 17 cases and among the bile duct carcinomas 24 gave definite evidence at autopsy of an icteric nephrosis. At necropsy these kidneys are swollen, deeply icteric, and have a very soft consistency.

Although metastasis of carcinoma of the gall bladder is generally accredited with being widespread and occurring early, the same concept is not applied to carcinoma of the extrahepatic bile ducts. In Marshall's series of bile duct cancers, about 25 per cent of his cases showed metastases. Renshaw stated that metastasis of cancers of the extrahepatic bile ducts "seldom occurs." He quotes the statistics of Devic and Gallavardin that metastatic growths were present in only 20 per cent of their cases. Musser lists to illustrate instances of metastasis in 18 such cases. Renshaw believed that distant metastases were rare and suggested that on laparotomy, "small nodules in the liver produced by peripheral dilatation of the small intrahepatic ducts may be mistaken for metastases." In our experience, 76.7 per cent of our cases of carcinoma of the extrahepatic bile ducts showed definite evidences of metastases and listing of the sites for metastases showed a diversity second only to carcinoma of the gall bladder.

The frequency with which certain sites are involved by metastases can be better appreciated by a short review of the lymphatic supply of the gall bladder and bile ducts. A plexus of lymphatics lies beneath both the mucosa and serosa of the gall bladder with short communicating vessels between them. The main lymphatic vessels drain to a sentinel lymph node usually located at the cystic duct. This lymph node receives similar afferent

lymphatics from the common bile duct, duodenum, and pancreas. Efferent lymphatic vessels extend from this lymph node up along the biliary tract and portal vein into the hilus of the liver. Therefore, a carcinoma of the gall bladder would tend to metastasize to the liver both by direct extension and by lymphatic spread. Bile duct carcinoma, on the other hand, extends first by way of the lymphatics, which in turn may involve adjacent organs. However, because of the close proximity of the hepatic ducts to the liver parenchyma, early direct extension may take place from that site. The lymph nodes involved are the cystic nodes, the peribiliary, peripancreatic, and periaortic nodes. The carcinoma may then spread to the mediastinal nodes, then to the tracheobronchial nodes, and finally to the supraclavicular lymph nodes. In that manner we frequently see a Virchow's node as in carcinoma of abdominal organs other than the stomach. Hematogenous dissemination undoubtedly occurs but is relatively infrequent. Distant metastases are much more common in our series than is usually reported. Table II shows the frequency with which the various sites were involved.

The 14 cases of carcinoma of the extrahepatic bile ducts without metastases were distributed as follows: 7 were located within the common bile duct, 5 involved the papilla of Vater, and 2 the common hepatic duct.

Analysis of the metastatic characteristics of the 2 neoplasms shows that the gall-bladder carcinomas tend to metastasize more frequently and to involve more structures. Undoubtedly this is largely due to its contiguity with the liver. Such distant metastases as the brain, heart, thyroid gland, and lung are indicative of a hematogenous spread. Although the right lower pulmonary lobe is supposed to be the most frequent site for pulmonary metastasis by way of the retrodiaphragmatic lymph nodes, enough other pulmonary lobes were involved to explain a hematogenous route. Although cases of Addison's disease have been reported by Warthin as due to the metastases of gall-bladder carcinoma, we have failed to find any in our material.

Among unusual symptoms produced by the metastases which complicated the diagnosis

TABLE II.—FREQUENCY AND SITE OF METASTASIS

Site of metastasis	55 cases of carcinoma of gall bladder No. cases	62 cases of carcinoma of extrahepatic bile ducts No. cases
No metastasis.....	2	14
Liver.....	51	35
Lymph nodes.....	34	28
Peritoneum.....	7	9
Omentum.....	10	4
Mesentery.....	8	4
Extrahepatic bile ducts.....	10	3
Gall bladder.....	0	4
Pancreas.....	3	10
Duodenum.....	3	4
Jejunum.....	1	0
Pylorus (stomach).....	1	2
Colon.....	6	0
Lungs.....	9	6
Adrenal.....	5	5
Kidney.....	3	1
Pleura.....	1	3
Rectum.....	2	2
Spleen.....	2	1
Diaphragm.....	1	1
Pouch of Douglas.....	3	0
Urinary bladder.....	1	0
Heart.....	1	0
Thyroid.....	1	0
Portal vein.....	1	0
Uterus.....	1	0
Umbilicus.....	1	0
Brain.....	1	0
Seminal vesicle.....	0	1
Skin of breast.....	0	1
Pancreatic duct.....	0	1
Ureter.....	0	2

we may list the case of a 37 year old colored woman who had an ulcerating lesion of the left breast which was treated as a scirrhous carcinoma. The area was treated with the x-ray prior to biopsy. The biopsy specimen suggested a metastatic hepatocellular carcinoma. The necropsy 1 year later revealed a medullary carcinoma of the common bile duct with metastases to the liver and skin of the left breast. One case of melanoblastoma of the gall bladder produced brain metastasis; the symptoms produced were attributed to central nervous system lues. None of our gall-bladder carcinomas metastasized to the ovary, which would label it a Krukenberg tumor. Such a case was reported by Shelley and Ross. Although Cooper, in his recent review of carcinoma of the papilla of Vater, quoted 20 per cent as the incidence of metastasis for that structure, we have found it to be 50 per cent.

The most common cause of exitus in these cases was found to be cholemia which is

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associated with cachexia and carcinomatosis in the majority of cases. Death is usually precipitated by an intercurrent bronchopneumonia. The less frequent causes of death occurred in the following order of importance: carcinomatosis and cachexia without cholemia, peritonitis due to various causes already described, bronchopneumonia, post-operative shock, and spontaneous hemorrhage.

## TREATMENT

Nothing more than disappointing results can be expected in the treatment of a disease inherently so difficult to diagnose as carcinoma of the gall bladder, especially in an early stage when treatment might be of some avail. To be sure the picture here presented is a gloomy one, for it is only the patients with unsatisfactory results who come to autopsy. We hope, however, that in revealing these frustrated attempts at surgical cure something may be gained from previous errors and a new method of procedure evolved.

Prophylactic removal of a diseased gall bladder affords faint hope in the treatment of carcinoma of that organ. In the hands of most surgeons the operative mortality following operations for cholelithiasis is less than that following operations for the removal of a carcinomatous gall bladder. Hence the possibility of the presence of a carcinoma of the gall bladder has been accepted by most surgeons as an indication for cholecystectomy. Erdmann's is the only dissenting voice in this popular opinion, for in his experience contrary to that of all others, the operative mortality following operation for cholelithiasis was as great as that for carcinoma. Judd and Baumgartner attributed the decreased incidence of carcinoma in surgical gall bladders of from 5 per cent to less than 0.5 per cent at the Mayo clinic to the earlier removal of diseased gall bladders.

Duodenal drainage together with repeated serum bilirubin determinations are of use in deciding upon the urgency for surgery. If no bile is recovered on repeated duodenal aspirations and the serum bilirubin remains high or every disadvantage in delaying operation. But, if occlusion of the biliary tract is only

partial as shown by recovery of bile on aspiration and there is a decline in the serum bilirubin, some time may be devoted to pre-operative therapy such as the administration of fluids, proteins, and vitamins. With the newer methods of controlling the hemorrhagic tendencies associated with icterus, surgical mortality should be materially reduced. Pall in 1921, attributed one-half of 25 immediate postoperative deaths in 31 operative cases of carcinoma of the bile ducts to postoperative hemorrhage. The same author has stated that the danger from cholemia is not great until icterus has persisted for from  $3\frac{1}{2}$  to 4 weeks and therefore that surgery should be attempted within 3 weeks of the onset of unremittent jaundice. The use of duodenal aspiration to differentiate carcinoma from cholelithiasis, and carcinoma of the ducts from carcinoma of the head of the pancreas, is fraught with considerable inaccuracy. An impacted stone may produce the same clinical picture as a neoplasm, and we have seen a carcinoma of the head of the pancreas occlude the common bile duct by metastasizing long before it had produced obstruction of its own duct.

Not only is the clinical diagnosis difficult but accurate location of the primary lesion even at the time of laparotomy is fraught with considerable difficulty, especially when the lesions involve the lowermost portions of the common bile duct and the papilla of Vater. We have found 5 instances in our series in which laparotomies performed by capable surgeons revealed what was thought to be carcinoma of the head of the pancreas but at post-mortem examination was proved to be a carcinoma of the extrahepatic bile ducts. The error, we believe, lies in the popular misconception of the relative frequency of these two lesions and in the fact that a normal pancreas frequently feels exceedingly hard. We have already stated that in our series of cases, we have found that carcinoma of the head of the pancreas is a poor third as the etiological agent of malignant obstruction of the biliary tract. Moreover, experience at the necropsy table reveals that an apparently normal pancreatic gland is frequently hard in consistency. The picture is further complicated by the

tendency for fibrotic changes to occur within the pancreas in cases of obstructive jaundice.

In 3 of our 55 cases of carcinoma of the gall bladder cholecystectomy had been carried out at least 6 months prior to the onset of the present illness. Cholecystostomy was carried out in 2 cases and jejunostomy in 1, as palliative procedures. Nature was kind to 8 of the 55 cases in which a spontaneous cholecystocolostomy or cholecystoduodenostomy occurred, but the success of this procedure was short-lived in 3 of these cases, for the patients died soon after of biliary peritonitis.

Cholecystostomy was performed in 5 of the 62 patients with bile duct carcinoma, cholecystogastrostomy for another 4 patients, and cholecystoduodenostomy for still another. One of these patients had in addition to a carcinoma of the common bile duct an independent primary carcinoma of the pylorus of the stomach; the latter neoplasm was the one recognized at laparotomy, and the widespread metastases which were found at that time were believed to be due to it but later proved to be due to the carcinoma of the bile duct. Radical resection of the involved parts was not attempted in any of our cases. It is, indeed, a formidable procedure from which recovery is a singular feat. The palliative procedure of biliary enteric anastomosis overcomes the complication of cholemia, gall-bladder infection, and cholangitis, and decreases the spasm of the duct by eliminating the back pressure of a distended gall bladder.

#### SUMMARY

From a series of 13,300 consecutive autopsies, of which 1,808 were primary malignant neoplasms, we have presented 55 cases of carcinoma of the gall bladder and 62 cases of carcinoma of the extrahepatic bile ducts. Of our cases of carcinoma of the gall bladder 76.4 per cent were in the female, usually within the sixth or seventh decades; 55 per cent of our cases of carcinoma of the extrahepatic bile ducts were in the male of similar average age.

The clinical syndrome associated with these lesions is not as simple as commonly believed which fact probably explains the frequently incorrect diagnosis. Pain was present in 60 per cent of the cases of gall-bladder carcinoma.

Jaundice was present in another 60 per cent of these cases, and gastrointestinal symptoms and cachexia in about 50 per cent. Evidence of edema and ascites was seen in 40 per cent. A palpable liver was found in 63 per cent of these cases whereas a palpable gall bladder was seen in 23 per cent. A profound secondary anemia was the only consistent laboratory finding, being present in 36 per cent of these cases. Of these patients 30 per cent gave a history of previous gall-bladder disease.

Pain of a less severe character was present in 42 per cent of our cases of carcinoma of the extrahepatic bile ducts. Jaundice was seen in 92 per cent and gastrointestinal and cachectic symptoms were elicited in approximately 50 per cent of them. A palpable liver was found in 60 per cent of this group whereas a palpable gall bladder was present in 30 per cent. Approximately 50 per cent of this group gave evidence of edema and ascites. A severe secondary anemia was observed in 30 per cent and chemical blood in the stools in 55 per cent of these patients.

An infiltrating adenocarcinoma is the most frequent type of carcinoma in these neoplasms, a papillary adenocarcinoma being the second most common. Next in order of frequency were the following: scirrhus adenocarcinoma, medullary carcinoma, mucus-producing adenocarcinoma, sarcoma, and one example each of squamous cell carcinoma, round cell carcinoma, and melanoblastoma.

Among the complications of the neoplasm, biliary cirrhosis was by far the most common, followed by cholangitis, empyema of the gall bladder, pericholecystic abscess, liver abscess, hydrops of the gall bladder, biliary peritonitis, spontaneous perforation, and fat necrosis or atrophic fibrosis of the pancreas. Of 55 cases of gall-bladder carcinoma, 36.3 per cent gave evidences of cholecystitis and 72.6 per cent of cholelithiasis. In 3 per cent of the calculous gall bladders a malignancy was present; in 30.6 per cent of the 62 cases of bile duct cancer gallstones were found, and in 22.5 per cent there was evidence of cholecystitis.

In our experience, Courvoisier's law is verified more often by post-mortem examination than by clinical findings; nevertheless, even



## SURGERY, GYNECOLOGY AND OBSTETRICS

- autopsy records indicate the inaccuracy of this didactic principle. A distended gall bladder was found in 29 per cent of the necropsies of gall-bladder cancer, and in 62.9 per cent of the necropsies of bile duct cancer.
- Evidences of metastases were found at necropsy, varying from involvement of the regional lymph nodes to generalized carcinomatosis, in 96 per cent of our cases of gall-bladder cancer and in 76.7 per cent of bile duct cancers. The liver was the most common site for metastasis. Several examples of hematogenous spread were seen. The tendency for metastasis was not characteristic of any particular histological type of neoplasm. To date, the surgical treatment of this disease has been unsatisfactory and chiefly limited to palliative procedures.
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# EDITORIALS

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## SURGERY Gynecology and Obstetrics

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NOVEMBER, 1941

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### THE TUMOR CLINIC IN TEACHING HOSPITALS

**D**URING the past ten years, one of the noteworthy achievements of the American College of Surgeons has been the establishment and organization of the cancer clinic in a large number of the country's general hospitals. At the beginning of this program a minimum standard for cancer clinics was agreed upon and since that time yearly reports have been prepared and published, listing those hospitals which conduct cancer clinics in accordance with the requirements of the College. From a small start this list of approved clinics has steadily increased in size, until, in 1940, it contained the names of nearly 350 hospitals. As a result of the many approved clinics now available throughout the country, and also due to the publicity given them through the various educational programs, vast numbers of cancer patients have benefited enormously. The results of recent cancer research are made available to them, adequate facilities for proper

treatment are provided, and the recommendations in each case represent a composite opinion of a group of interested and well trained specialists.

Since many of these cancer clinics have now been in existence long enough for the period of adjustment to have been completed and also for those in charge to have accumulated considerable experience in their management, it is perhaps not amiss to view in retrospect the tumor clinic as it operates in the large general hospitals with medical school affiliations and to appraise this work from the standpoint of the several functions of the hospital and the school.

While the details of organization and conduct of such a clinic may differ in different environments, fundamentally the problems are essentially the same. At the University of Michigan the cancer clinic is under the supervision of a cancer commission or committee created by regential action, and composed of the following specialists, each of whom holds a position of professorial rank in the medical school: pathologist, radiologist, surgeon, internist, gynecologist, urologist, ophthalmologist, otolaryngologist, orthopedic surgeon, dermatologist, neurosurgeon, thoracic surgeon, and an executive officer. Generally speaking the function of this committee is to coordinate and correlate all of the various agencies of the hospital and medical school for the purpose of affording patients afflicted with malignant neoplasms the best possible professional service, whether the problem is one of early and correct diagnosis or exclusively one of treatment. The committee aims to integrate and consolidate the experiences of the entire staff in all matters pertaining to malignant

## SURGERY, GYNECOLOGY AND OBSTETRICS

neoplasms, to evaluate existing forms of therapy, and to consider judiciously certain newer methods thought to be worthy of clinical trial.

By means of a close liaison with the social service department and through the assistance of its representatives, provision is made for a thorough and continued follow-up study of cancer patients for the remainder of their lives.

In order to make the data assembled from many sources readily available for study and analysis, a central record system becomes essential. Clinical investigation is thus fostered and in addition to the many special studies constantly in progress, yearly reports of the hospital's cancer experience contain much significant information.

Important among the several activities of the cancer clinic are the clinical sessions or conferences. By means of regularly scheduled tumor conferences, provision is made for centralized, prompt, and efficient consultation service which is available to all of the clinical departments. At the time of the conference all relevant data, for example, x-ray films and microscopic preparations, are available for examination by those in attendance and an expert is present to interpret them. Informal discussion is encouraged and the consultation happily loses much of the austere formality which is unavoidable under the refer system. Each conference is regularly attended by a representative from the departments of surgery, pathology, and radiology. The departments of otolaryngology, ophthalmology, dermatology, medicine, pediatrics, oral surgery, and neurology are represented when patients from these services are presented.

While no attempt is made to usurp the right of any individual department to treat patients regularly assigned to it, as deemed best, nevertheless an attempt is made to bring about a

standardized plan of clinical procedure in the matter of handling cancer patients. As the result of these conference gatherings, group opinion on various phases of cancer management begins to crystallize and programs of treatment are developed. At the conferences the joint opinion of the pathologist, the radiologist, and the medical and surgical specialists are expressed in writing for the hospital record before treatment is begun. Information regarding biopsy, various palliative and curative surgical procedures, and the employment of radiation methods becomes widely disseminated throughout the staff. Patients seem to appreciate the thorough individual attention which they receive and, as a rule, are impressed with the judgment and advice handed down by the conference group.

Medical students in small groups attend a certain number of these conferences. By so doing in a limited period of time it is possible for them to witness many more unusual and interesting lesions than would be possible during their regular tour of duty on the wards and in the dispensaries of the various departments. Moreover, they learn from the informal discussions that clinical medicine is not a static affair but that there are differences of opinion among mature and well trained clinicians, and they become aware of the progress which is being made in medicine, as they observe certain changes in policy regarding treatment being put into effect.

Staff members conducting the conferences and attending regularly also are afforded an opportunity to observe a large number of uncommon neoplasms, an experience which provides an excellent background of material with which to elucidate subsequent didactic lectures and systematic presentations. In addition these tumor conferences are important in the field of postgraduate medical education. Referring physicians knowing about the con-

ferences often find it worthwhile to accompany their patients or to attend periodically. As a part in the clinical programs arranged for various visiting medical groups, a "sample" tumor conference has proved to be a popular and instructive exercise. These conferences and the preparations for them, involve a considerable amount of work. Lists of the cases to be presented at each conference must be prepared; periodic reports must be written as to status of patients previously seen by group; social service contact with patients must be made, lesions as they appear at the conference must be photographed, and conference opinions filed in each patient's case record.

The success of the conference depends largely upon the regular attendance, enthusiasm, and energy of those in charge, and upon the co-operation of all members of the staff.

Since there is a certain stigma attached to the term "cancer conference," and since the term "tumor conference" may be objectionable to patients for the same aesthetic reasons, various substitutes have been suggested. "Oncology clinic" is preferred by some. In our own hospital we have agreed upon "Neoplasm Conference," a term which seems to be without opprobrium and which, at the same time, is simple and descriptive.

From this brief review, it becomes quite evident that in its own right, the cancer clinic fulfils well the three important functions of a hospital to which Osler so often referred, namely: the care of the patient, the instruction of the students, and the extension of knowledge.

HENRY K. RANSOM.

## COMPOUND FRACTURES AND WOUNDS IN WAR

A CONVERSATION with any of the leaders of surgery in North America today does not have to be a prolonged one to reveal that their minds are much

occupied with the practice of their profession under military conditions. Some are engaged in problems of organization, some in problems of surgical research, some in the selection of surgical methods that are to be recommended, and some in the incorporation of all of these phases in manuals of procedure. Civilian surgeons are co-operating to the fullest extent with those in the medical service of the military branches of our Government to assure our soldiers and sailors the best that North American surgery has to offer.

It has been emphasized by Dr. Sumner L. Koch in a recent editorial<sup>1</sup> in SURGERY, GYNECOLOGY AND OBSTETRICS that war surgery differs from peace time surgery only in the conditions under which it is practiced and that not in any way is there a difference in the surgical principles which must be observed. It is true that the exigencies of time and the distances through which wounded men may have to be transported may not permit the immediate application of methods that would constitute first measures under ordinary civil conditions, but this fact in no way invalidates the surgical principles involved.

The Committee of the American College of Surgeons on Fractures and Other Traumas made the treatment of compound fractures and wounds of soft parts its major subject of discussion at its annual meeting in New Orleans, January, 1941. Its discussion culminated in a resolution on these subjects, and the distinguished personnel of that committee commands serious consideration of its conclusions.

The Committee on Fractures and Other Traumas, of the American College of Surgeons, at its executive session in New Orleans, January 11, 1941, adopted the following resolutions in reference to the treatment of compound fractures and wounds in war.

<sup>1</sup>Surg., Gynec. & Obst., 1941, 72: 672-673.

## SURGERY, GYNECOLOGY AND OBSTETRICS

## COMPOUND FRACTURES

RESOLVED: That it is the consensus of this Committee that the use of snug-fitting plaster encasements in the initial treatment of acute compound fractures is inadvisable except where the case can be closely and continuously observed.

That early splinting, utilizing fixed traction, should be followed by adequate débridement at the earliest possible time; that such débridement should accomplish removal of all dead and devitalized tissue, eliminating all dead spaces and removing all foreign material.

If chemical sterilization is feasible, the use of aqueous sodium hypochlorite is advised.

That the immediate closure of compound fractures is inadvisable.

## WOUNDS

That wounds of soft parts not involving bone, joint, nerve, or tendon, following mechanical and chemical débridement may be closed by secondary suture when the bacteriological check on the wounds proves it permissible. It is also recommended that the surgical committee of the National Research Council further consider the problem of improving and simplifying practices and procedures after a thorough study of the end-results of cases treated to date and a survey of all available literature.

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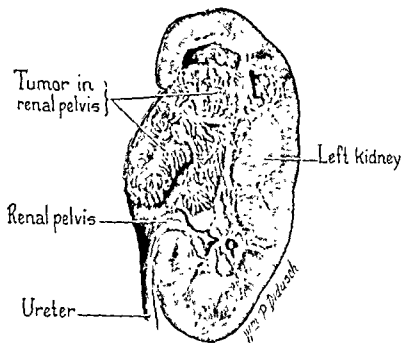


Fig. 1. Papillary carcinoma of the renal pelvis.

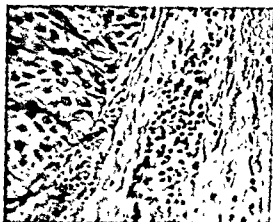


Fig. 6. Section from left renal pelvis showing typical papillary tumor structure.



Fig. 7. Section from cortex adjacent to papillary tumor, the tissue is entirely normal.

# SURGERY

## GYNECOLOGY AND OBSTETRICS

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### PAPILLARY CARCINOMA OF THE RENAL PELVIS

#### Diagnosis and Treatment

THOMAS J. KIRWIN, M.D., F.A.C.S., New York, New York

NO more than 10 years ago papillary carcinoma of the renal pelvis was looked upon as a very rare lesion.

But during the past decade an increasingly large number of these renal growths has been put on record, so that their occurrence can no longer be regarded as uncommon. It is probable that this increase in incidence is more apparent than real. The employment of improved methods of urologic diagnosis has made it possible to detect the existence of these growths in the living unoperated upon patient, and this in turn, has increased our knowledge of the pathological and clinical manifestations of all types of renal tumors, papillary epithelioma among them.

Up to the beginning of the present century the great majority of these tumors were recognized only at autopsy. The classic monograph of Albarran and Imbert, published in 1903, wherein the literature up to that date was thoroughly reviewed, listed but 42 tumors of the renal pelvis in a total of 585 renal tumors of all kinds. Of these but 18 were of the papillary type. Statistics of the Mayo Clinic from 1905 to 1922 showed but 13 renal pelvic tumors, of which but 8 were of the papillary type (7). In 1927 when Hunt made a further report from this same clinic, the number of

papillary tumors of the renal pelvis had risen to 15. In 1933, Kimball and Ferris from our clinic at the Brady Foundation collected 72 cases from literature, to which they added 2 more seen in their own service. In the 8 years which have elapsed since their paper was written, we have seen 3 cases of benign renal pelvic papilloma, and 4 malignant growths of the same nature. Writing in 1939, F. P. Johnson placed the incidence of papillary carcinoma of the renal pelvis at 4.9 per cent of all tumors of the kidney.

#### ETIOLOGY

Though we have no positive evidence concerning the origin of papillary carcinoma in the pelvis of the kidney, there is a strong probability that long continued irritation and inflammation may have some influence in its production. Stone, however, has never been put forward as a primary etiological factor; though it is occasionally mentioned, the coincidence is not frequent enough to permit any definite conclusions to be drawn. It seems more likely that the calculi were produced by the same conditions which favored the papillary growth. Scholl quotes Orth as having expressed the opinion that papillary or villous inflammation may be the initial form of what later becomes a papillary growth—that it merges into it and cannot be histologically dis-

From the Department of Urology, James Buchanan Brady Foundation, of the New York Hospital, New York.



tinguished from true papillary tumor. When the apparently uninvolved mucosa and submucosa bordering on the papillomatous area were microscopically examined, small villous processes, apparently inflammatory, were often found which were of a distinctly different type from the villous processes usually seen in connection with calculus formation of inflammation which has been confined to the epithelial layer. But at times the papillary processes will be found to involve the submucosa as well. When this occurs the submucosa will almost always show inflammatory reaction by the growth of fibrous tissue, attenuation of the walls of the blood vessels, granulation tissue formation, and the presence of round and plasma cells. The cellular tissue proliferation eventually leading to papillary carcinoma may arise from a regenerative fibrosis which takes place after inflammatory injury to the epithelium, or walls of the blood vessels. An excessive overgrowth of epithelium under these circumstances might produce such formations.

#### **PATHOLOGY**

Pathological reports vary considerably, probably because different investigators see the growths in all stages of development. One that was "only moderately rapidly growing" with a "fairly mature type of cell," seen by Hunt and Bennett, had the pelvic mucosa covered by a stratified layer of epithelium of irregular contour because of the many branched and anastomosing stalks which projected into the lumen of the renal pelvis. The epithelium was supported by a very delicate stroma which showed no tendency toward infiltration of the wall. Individually, the cells were large, their cytoplasm abundant, and their vesicular nuclei rather large. The cells of the basal layer were cuboid, but superficially more were of fusiform or spindle shape. Many perivascular lymphoid deposits were seen in the hypertrophied fibromuscular wall.

The growths are most often found at the ureteropelvic junction, and for this reason the ureter is likely to be invaded very shortly. If growth is at all vigorous, the renal pelvis is rapidly filled and the ureter may be involved by direct extension, or by transplants carried down in the normal process of urine excretion.

Henry Wade has said that "papilloma of the renal pelvis may be regarded as an innocent newgrowth possessing a very high degree of potential malignancy." He describes it as growing from the lining membrane of the renal pelvis or calyces into the lumen of the channel without invading the renal parenchyma. The delicate branching villi consist of a central core of connective tissue cells with large blood vessels, both covered by transitional epithelium. When malignancy begins in a previously benign growth, the change will first be noticeable in the cells at the base, and for a long time thereafter examination of the peripheral villi will show them still without any malignant characteristics. This emphasizes the importance of taking biopsy specimens from the full height of the growth, or better still obtaining more than one specimen from different portions. Only thus can the true nature of a neoplasm be recognized.

#### **SYMPTOMS**

The single symptom characteristic of all cases is intermittent hematuria, and this is common to so many other lesions of the upper urinary tract that it cannot be relied on to indicate that a pelvic tumor is present. Often the appearance of blood in the urine has been noted by the patient at intervals during several years previously. There is no pain and the patients are, as a rule, in good physical condition, until such time as the growth has advanced far enough to obstruct the outflow of urine, or to produce pressure symptoms, and when these symptoms are in evidence, the growth is usually too far advanced to permit adequate treatment. Therefore, the appearance of blood in the urine should always be looked upon as a grave matter, and every means available be put into use to discover its source. If this were a never varying rule of all physicians, renal neoplasms would be recognized much earlier than is now the case, and many lives, now being needlessly sacrificed, would be saved.

#### **DIAGNOSIS**

The history seldom contains anything more than the occasional occurrence of painless hematuria. A marked increase in the amount

of blood is usually what brings the patient for urological examination. The growth seldom enlarges the kidney enough to make its palpation possible. When the cystoscope is brought into use it is not uncommon to find a secondary papilloma—or a group of many—in the bladder, and the examiner may be satisfied that this is the source of the bleeding and investigate no further. The necessity for *complete* urological examination is thus emphasized. If ureteral catheters are passed during cystoscopy the affected side *may* yield blood-stained urine, but this is by no means the rule. If the instrumentation is skillfully done, the impact of the catheter upon the villi of the growth often causes no hemorrhage, and if a plain x-ray film be made while the catheter is still in the ureter, it is not likely to show anything abnormal. Even when an opaque medium is injected it may not be possible to detect any change from the normal outline of the pelvis and calyces. Wade suggests, however, that a very careful inspection of such an x-ray

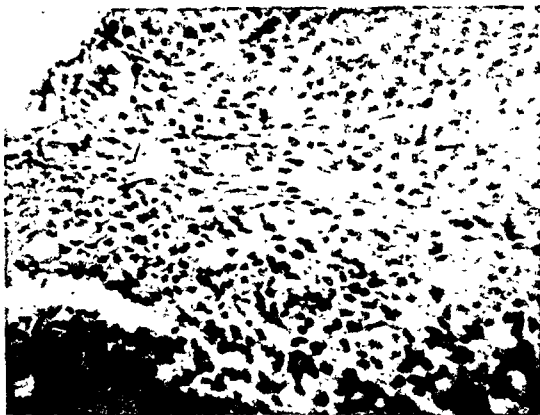


Fig. 2. Diagnosis by aspiration: photomicrograph of material aspirated by method of Vincent Archer (case of Dr. Samuel A. Vest).

film will show that "the density of the opacity within the pelvis is seen to vary, and thus the shadow outline of the growth within the cavity is obtained. A delicate soft photograph is required to demonstrate this appearance, and



Fig. 3.

Fig. 3. Excretory pyelogram showing the superior calyx pushed downward, suggesting a tumor mass. Impression heightened by definite defect in pelvic outline: Inferior calyx, though within normal limits, is displaced slightly



Fig. 4.

downward, a factor also suggesting the presence of mass pressure from above.

Fig. 4. Retrograde pyelogram, with findings practically identical with those shown in Figure 3.



Fig 5. Kidney injected after nephrectomy. Note how calyces are pushed downward by the tumor mass

it is well worth while to repeat the injection to confirm this observation if doubt exists, as the appearance is dependent on the density of the tumor being less than that of the pyelographic medium, and thus the diagnosis rests on the demonstration of a slight alteration in the density of the shadow." But if a filling defect can be recognized, the diagnosis can usually be established, when taken in connection with the previous findings. Differentiation from renal tuberculosis or stone will, however, at times prove troublesome.

**Diagnosis by aspiration** In one of his last publications, the late John Roberts Caulk suggested that in the diagnosis of pelvic neoplasms "the microscopic examination of bits of tissue in the urine or examination of washings from the renal pelvis with recovery of tumor cells will prove of great assistance." This idea has been elaborated by Dr. Vincent Archer, roentgenologist at the University of

Virginia Hospital. In a case seen in the department of urology at that institution, Dr Kirby, after making the pyelogram, left the catheter in the pelvis where a papillary growth was suspected, and "forcibly aspirated" material for microscopic study. The cells thus secured were many of them "obviously malignant" and "there was even a suggestion of papillary growth"—most valuable confirmatory evidence for the pyelographic diagnosis (Fig 2).

**Excretion urography.** For the diagnosis of renal pelvic growths, excretion urography is very seldom as satisfactory as the retrograde method. This is because the function of the affected kidney is usually so reduced that it cannot excrete enough of the contrast medium to produce clear roentgenograms. Therefore, unless it be positively contraindicated, the older method should always be used. In the case herein reported both methods were employed, but because function in the affected kidney had remained remarkably good there is practically no difference between them (Figs. 2 and 3).

#### PROGNOSIS

The outlook for the patient proved to be harboring a papillary growth of the renal pelvis is hedged about with many "ifs" and "buts." So far, no rule has been laid down by which we may even attempt to estimate the chance of recurrence after surgical removal, nor have we discovered any law governing the frequency with which benign lesions may become malignant. But as a general rule, recurrence is likely, and untreated benign papilloma will eventually become malignant. Therefore, all papillomas of the renal pelvis should be looked upon as potentially, if not actually, malignant and should be dealt with accordingly.

#### TREATMENT

In general, tumors of the renal pelvis are classed as "radioresistant," and the majority of urologists consider complete surgical removal of the affected kidney to be the only safe course. Caulk and some others have advocated preliminary roentgen therapy, believing that there would be less danger of dis-

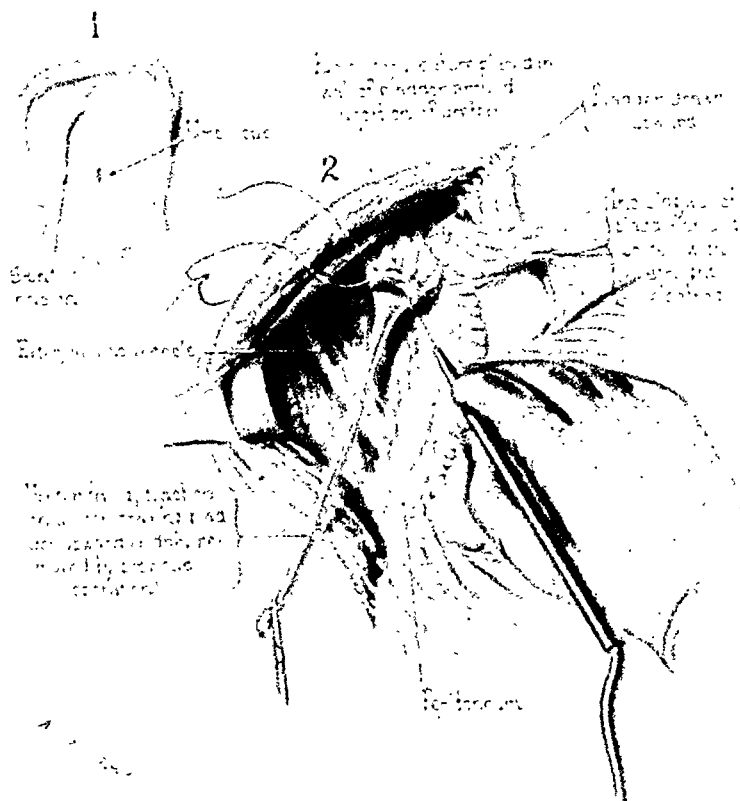


Fig. 8. Left ureterectomy, secondary to left nephrectomy. 1, Skin incision. 2, Ureter freed and withdrawn from wound, traction exerted on ureter draws bladder upward. Purse string suture placed in bladder wall, encircling insertion of left ureter. With a straight-wire electrode, bladder wall is incised, a cuff of healthy mucosa being left attached to excised ureter.

semination of the tumor cells when nephrectomy was carried out. Postoperative x-ray and the implantation of radon seeds have likewise been advocated and practiced. But Waters, of the Brady Urological Institute of Johns Hopkins University, who has had an exceptionally wide experience in urological roentgenography, has pointed out that as all renal pelvic growths tend toward the squamous cell type, in that they are not derived from transitional epithelium, they are inevitably resistant to radiotherapy and cannot be expected to show as good results from this therapy as do the larger cortical growths of the kidney.

Because metastasis or extension to the ureter is so common an occurrence in malignant pelvic growths, complete nephroureterectomy

is, in my opinion, the only safe course to pursue. This is often done at a single operation, because of fear that tumor cells may be disseminated by the first—incomplete—step of the procedure. Pathological investigation has shown that malignancy readily spreads by implantation to the ureteral mucosa, often reaching the bladder, where secondary growths may appear around the ureteral meatus.

This same danger makes simple nephrectomy an inadequate measure for dealing with these pelvic growths. Early in the present century surgeons began not only removing the kidney and upper third of the ureter, but extirpating the entire upper urinary tract, including a "cuff" of vesical mucosa surrounding the meatus of the operated ureter. But, as J. A. C. Colston has said, "This operation

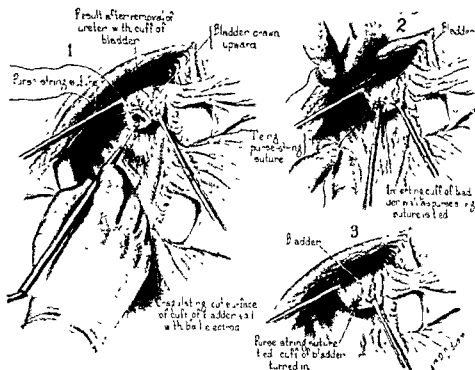


Fig. 9. Left ureterectomy, secondary to left nephrectomy. 1, Ureter removed, traction on bladder by means of Allis clamps, coagulation of cut edge of bladder by ball electrode. 2, Tying of purse string suture inverts cut edges into bladder cavity. 3, Tying of purse string suture has effectively closed opening in bladder wall left by removal of ureter.

is a rather formidable procedure, is taxing on many patients and, particularly in obese individuals, satisfactory exposure of the lower end of the ureter as it enters the bladder, may present serious technical difficulties. It has further been found that the suture in the bladder wall may slough leading to troublesome urinary fistulae, and the possibility of deep-seated infection in a locality which is hard to drain. Colston conceived the idea of using the electrocautery knife for the excision, thus minimizing the danger of malignant transplants. Also this method took less time, and was better borne by much enfeebled patients.

#### CASE REPORT

A woman 41 years old entered the James Buchanan Brady Foundation for Urology on March 8, 1910. She gave a history of painless hematuria at intervals of about 48 hours for 2 weeks past, no other urological symptoms. The physical examination revealed nothing abnormal and no red blood cells

appeared in the urine at this time. Cystoscopy was done with the flat plate and bilateral pyelograms and pyeloureterograms, giving an impression of tumor at the superior pole of the left kidney. Excretory ureterograms obtained 3 days later showed the same morphology as had the retrograde investigation. A mass in the upper pole of the left kidney seemed to be pushing the middle group of calyces downward (Fig. 4). Upon these findings a diagnosis of tumor of the left kidney was made, and left nephrectomy carried out. Convalescence was uneventful, the patient being discharged on the sixteenth postoperative day, to return later for ureterectomy. The pathological diagnosis was papillary carcinoma of the renal pelvis. The sectioned kidney is shown in the colored plate (Fig. 1). The papillomatous mass occupied the upper two-thirds of the left pelvis, as well as the calyces in the upper part of the kidney. The papillae were flattened and the epithelium of the calyces replaced by tumor growth (Fig. 6). A smooth lined cyst approximately 2 millimeters in diameter occupied the lower pole of the left kidney. The remainder of the left kidney was entirely normal (Fig. 7). The 4 centimeter length of ureter which had been removed with the kidney showed no evidence of carcinoma, though the subepithelial tis-

sue was edematous and infiltrated with leucocytes, as were the muscles also. Numerous hemorrhages were in evidence in the wall and in the submucosa.

On April 23, 1940, 6 weeks after the first operation, the patient re-entered the Brady Foundation for secondary ureterectomy. There had been no urinary symptoms during the interval, and the physical and laboratory findings were essentially negative. Under avertin and gas oxygen anesthesia incision was made along the outer border of the left rectus muscle, incurving toward the median line (Fig. 8, 1), exposing the ureter, which was freed and drawn from the wound. Traction was exerted upon the ureter in such a manner as to draw the bladder upward. A purse-string suture was run around the bladder at its vesical insertion. By use of a straight-wire electrode the ureter was then freed from the bladder wall, and a cuff of healthy tissue was left completely encircling it (Fig. 8, 2).

After removal of the ureter, traction was maintained upon the bladder by means of Allis clamps. The cut edge above the purse-string suture was carefully coagulated with the ball electrode to prevent any possible dissemination of tumor cells (Fig. 9, 1). The suture was then gradually drawn together, everting the cut edges within the bladder cavity as the orifice left by the ureter's removal was obliterated (Fig. 9, 2). In Figure 9, 3, may be seen the outside appearance of the bladder after the purse-string suture was tied. This procedure, while following the technique of Colston quite closely, differs in that he merely coagulated the stump of the ureter where it had been cut off on the external surface of the bladder wall. He did not remove a precautionary "cuff" of healthy vesical mucosa, nor did he make use of the purse-string suture to draw up and evert the opening in the bladder wall.

*Pathological report on the ureter.* Sections taken at 1 centimeter intervals throughout the length of the excised ureter gave no evidence of carcinoma, though in one section there was a small papillary projection of the epithelium. Throughout the subepithelial tissue there was an occasional area of infiltration, and still more rarely, an invasion by polymorphonuclear leucocytes. The ureter was hyperemic throughout, with several areas of frank hemorrhage, but nowhere was malignancy in evidence.

*Prognosis* in this case is very good, as the patient, so far, remains in excellent condition. Though Ewing states that metastases are often observed in adjoining nodes or in the adrenal, in the peritoneum or other neighboring structures, careful search has, in this case, revealed nothing of the kind. We believe, however, that the precaution of secondary complete removal of the ureter was well taken, even though it proved *not* to contain any malignant extension of the pelvic growth. The well known tendency of "benign" papillomas

to become malignant, and the evidence of a pronounced chronic ureteritis give ground for the assumption that, had the ureter been left *in situ*, malignancy would eventually have occurred.

#### SUMMARY

Papillary carcinoma of the renal pelvis is a relatively uncommon form of neoplasm, though a steadily increasing incidence would seem to be indicated by the number of reports concerning it which have recently appeared in medical literature. This is due, however, not so much to actual increase in the number of cases, as to improvements in urological diagnostic methods, which permit more frequent recognition of the lesion.

The embryonic relationship between the ureter and the renal pelvis is much closer than the ureter's structural affinity to the kidney proper. Therefore, neoplastic growth in the renal pelvis extends rather to the ureter than to the renal cortex.

For this reason, the hope of permanent removal of the disease lies in surgical extirpation of both kidney and ureter, even if no active proliferation can be detected in the ureteral mucosa. Complete nephroureterectomy is the only answer to the surgical problem. This may be done in either one or two stages.

A case report is presented in which a modification of Colston's procedure is described.

The results achieved in this case give ground for the belief that no time should be wasted in the application of x-ray therapy. Coutard's method of fractional dosage was attempted, but the patient proved unable to endure it. We have no reason to think that her present condition would be in any way better had the full dosage demanded by this therapy been administered.

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# THE GASTROINTESTINAL TRACT IN HYPERTHYROIDISM

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**D**IGESTIVE disturbances in hyperthyroidism are often so overshadowed by cardiovascular, neuromuscular, or ocular manifestations that they are not given proper consideration. Hyperthyroidism may not be recognized when the symptoms are chiefly gastrointestinal. Frequently in this type of thyrotoxicosis, as exemplified by a series of 34 cases reported by Verbycke, there is little or no clinical evidence of thyroid enlargement. Only when the physician has been educated to the causal relationship between hyperthyroidism and digestive disturbances is the basal metabolic reading requested and the diagnosis established.

As early as 1896 Moebius wrote of diarrhea as an important symptom of Basedow's disease. He regarded the diarrhea as an attempt on the part of the body to eliminate a toxin with which it was overladen. Many other ingenious but equally unproved explanations for the diarrhea of thyrotoxicosis have been advanced (16, 22).

Increase in appetite, nausea and vomiting, and even abdominal pain may be manifestations of hyperthyroidism. Although loss of weight may be dependent in part upon gastrointestinal disturbances, it should not be considered primarily a gastrointestinal symptom. It is more directly related to an increase in metabolism and to the effects of a vitamin B complex deficiency (17, 21, 43).

An idea as to the frequency of occurrence of these gastrointestinal symptoms may be obtained from the following statistics Verbycke, in his 34 cases of hyperthyroidism with predominant gastrointestinal symptoms, found abdominal pain as a chief complaint in 16, nausea and vomiting in 9, gas in 5, and

diarrhea in 3. Shirer found diarrhea in 14 per cent of 42 patients studied, constipation in 31 per cent, and normal bowel habits in 55 per cent. Tinker (51) reported digestive disturbances in 1,415 of 4,127 cases of goiter. Persistent diarrhea was present in 10 per cent of these patients, nausea and vomiting in 10 per cent.

Although the occurrence of gastrointestinal symptoms in hyperthyroidism is an established fact, the underlying disturbances in gastrointestinal physiology are too often only a matter of conjecture. Any study of these fundamental changes must of necessity be divided into two main groups: first, a study of secretory activity; second, a study of motor activity.

## GASTRIC SECRETION

In 1904 Miesowicz reported the absence of hydrochloric acid in the gastrointestinal secretions of 7 patients with Basedow's disease examined both in a fasting state and after a protein test meal. Since that time many authors have reported similar findings.

Wolpe studied 16 cases of Basedow's disease and found hypochylia or achylia in a majority. He found the greatest reduction in free acid in advanced cases. Badykies obtained similar results on administering dried thyroid to normal individuals. In a majority of the cases gastric secretion was diminished both in amount and in free and total acid content. These were the individuals with the most pronounced reaction to the thyroid medication, as judged chiefly by its effect on the cardiovascular system. In those with a mild reaction, gastric secretion was increased in amount.

Lerman and Means (29) found anacidity in 38 per cent of a group of 50 patients with exophthalmic goiter. They found that the achlorhydria became more frequent not only with increase in the basal metabolic rate but also with increase in age and severity of anemia. Moll and Scott (40), Wilkinson, and

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Schwanke, all found a high incidence of achlorhydria in hyperthyroidism but related it to duration rather than to severity of the disease. On the other hand, Alfred Brown found a greater percentage of achlorhydria in cases of short duration. Berryhill and Williams found achlorhydria in 69 per cent of 35 patients with exophthalmic goiter and 67 per cent of 15 patients with toxic adenomas. They found no correlation with age, duration of the disease, or metabolic rate. Leist found achylia in 2 and anacidity in 5 of 8 cases studied, even in the presence of concomitant hyperchloremia. He believed that these abnormalities in gastric secretion were related to the low protein content of the blood serum.

Lewit found hypoacidity in 4 and achylia in 5 of 10 patients with classical Basedow's disease. In addition he studied 17 cases of this disease which had come to autopsy. Atrophy of the gastric mucosa was present in 10 cases. On the basis of these findings Lewit postulated a form of achylia dependent on organic changes as well as one dependent on functional changes. Whatever the underlying cause for these disturbances in gastric secretion may be, the process is certainly not irreversible. In Berryhill and Williams' series, 73 per cent of the hyperthyroid cases with an initial achlorhydria showed, after treatment, a return of the gastric secretion to within normal limits. Wilkinson found that 22 of 25 cases of hyperthyroidism with a preoperative achlorhydria had free acid in the gastric contents when examined 3 months after operation.

Another group of investigators (11, 15, 32, 39, 45) did not find a high incidence of achlorhydria in the cases of hyperthyroidism studied by them. Normal values for free acid were obtained from the gastric secretions of patients with toxic adenomas studied by Moll and Scott (40). In 11 cases of *forme fruste* reported by Lewit the findings were similar. Still another group has reported high gastric acidity in thyrotoxic states (1, 7, 32, 34, 41, 45). Most cases of Basedow's disease showed hyperacidity in Boenheim's series, especially the early cases. Neilson found hyperacidity an early sign of hyperthyroidism. Badykies found this increase only in the weak reactor, and Boenheim only after a special test meal and

not after the Boas-Ewald meal. Maranon reported hyperchlorhydria in the "vagotonic form of hyperthyroidism" but not in the true Basedow's disease.

Experimental work in this field has yielded equally confusing results. Hardt, Truesdell, Chang and Sloan, all reported a decrease in gastric acid secretion in Pavlov pouch dogs which were fed thyroid substance. Moll and Flint (39) fed thyroid to 4 dogs with Janeway fistulas. They found achlorhydria in 2, slight hypochlorhydria in 1, and increase in acid in 1. Lewit observed an increase in the volume but no change in the acidity of postprandial gastric secretion in Pavlov pouch dogs after the administration of thyroïdin.

Although this review of the literature on gastric secretion in hyperthyroidism discloses many apparent discrepancies, we have at the same time received indications of certain factors which may explain in part this confusion of results. Friedman, with the work of Eppinger and Hess as a background, has postulated the presence of both sympathetic and vagal products in thyroid secretion. He has suggested that the effect on gastric secretion depends upon which fraction predominates. The severity of the thyroid intoxication, the duration of the disease, or the type of goiter may be modifying factors in the gastric secretory effects of hyperthyroidism.

There has been no standardization of the technique for gastric analyses through these many studies. Every conceivable type of test meal has been used; single and fractional specimens have been taken at varying time intervals; histamine was administered to some and not to others. Of significance in this connection are the observations of Eggleston (6) and of Bockus, Bank, and Willard. The former noted that the incidence of achlorhydria was twice as great by the single extraction as by the fractional method. The latter group went a step further to demonstrate that after histamine only 53 per cent of those showing achlorhydria with the Rehfuß fractional method failed to secrete acid.

Finally it is only in comparatively recent years that well controlled series of gastric analyses in normal patients have been available as standards of comparison (5, 6, 27, 30,





Fig 1a



Fig 1b



Fig 1c

Fig 1. Hyperthyroid patient No. 6, (preoperative)  
 a, An orthotomic stomach with very prominent gastric rugae. Emptying time, 5 hours and 30 minutes. b and c, Four plus small intestinal tone with a fine herringbone pattern. Note the transverse position of the upper jejunal loops which we believe is indicative of shortening. The barium reached the cecum in less than 1 hour.

influence gastric secretion have been discovered. Achlorhydria increases with age; its incidence is higher in females. A direct relationship has been found between the degree of gastric acidity and the physical fitness of the patient. Acidity also varied directly with the hemoglobin and red blood cell counts in one study (30).

#### GASTROINTESTINAL MOTOR ACTIVITY

Experiments performed *in vitro* (16, 21) to test the effect of thyroid preparations on excised intestinal muscle, although interesting, have little direct clinical application. The same may be said of the experiments of Boenheim and Wertenberger on frogs. Before proceeding to a consideration of the experimental work on mammals, we should prepare to evaluate the results in the light of the following findings of Carlson and co-workers (10).

50). As a result of these studies in normals, many physiological factors which definitely



Fig. 2a.



Fig. 2b.

Fig. 2. Same case as shown in Figure 1 (postoperative). a, Gastric rugae are less prominent. Although there apparently is more barium in the stomach at this postoperative examination, the amount given for these studies was always the same. Gastric emptying time was 3 hours and 6 minutes. b and c, Small intestinal tone is now classified as 2 to 3 plus. The pattern is coarse herringbone to "stacked coin" in appearance. The short transverse jejunal loops have disappeared.

Man was more susceptible to thyroid feeding than any of the animals studied. Herbivora were more susceptible than carnivora. No nervousness, tachycardia, or exophthalmos was produced in the laboratory animals. Loss of weight, gastroenteritis, and diarrhea were the most common symptoms in all.

Deutsch made window observations on living rabbits and found that thyroid preparations increased the motility of the whole gut without producing spasms or incoordinate movements. Perussé and Rozen studied the movements of the empty stomach in gastric fistula dogs after feeding of thyroid. Small dosages (2.5 grams daily) increased the hunger contractions in 4 of 5 dogs. Results with larger dosages were somewhat equivocal.

Fetter and Carlson (20) with balloon recording from the stomach and fluoroscopic ob-



Fig. 2c.

servation of the intestines studied the effect of thyroid substance on the gastrointestinal



Fig 3 Hyperthyroid patient No 10 (preoperative). Very prominent gastric rugae as viewed in silhouette along the greater curvature at a

tract of 6 dogs. Increased gastric motility and periods of increased tonus were observed in all dogs. As long as 2 months after the feeding of thyroid was stopped 4 of the dogs had not yet returned to normal as regards gastric motility. In 5 of the 6 dogs the stomach emptying time was shortened and the barium reached the colon earlier than in the normal. Barium remained in the colon the normal length of time in all but 1 dog. These investigators discussed several theories to explain this thyroid action, but felt that none was satisfactory. However, in a later set of experiments, Fetter, Barron, and Carlson (19) were of the opinion that they had proved that this thyroid effect was not due to an influence of the thyroid hormone on the gastrointestinal vagus mechanism.

Kratonoff studied dogs with chronic gastric and duodenal fistulas. In 4 of 6 dogs an increase of hunger contractions was observed after thyroid feeding. Intensity of effect depended within definite limits on dosage, and a tendency to develop tolerance was observed. The effects on gastric motility produced by a month's thyroid feeding persisted for at least 10 months after feeding was discontinued.

Finally we come to the observations on humans. With one or two possible exceptions these have been incomplete and often conflicting. Lorenzi found gastric digestion speeded up in 6 cases of hyperthyroidism studied by him. Radiological observations on the rupture of a bismuth filled gelatin capsule served as an indicator. McCarrison stated that dilation of the stomach is a frequent accompaniment of Graves' disease. On the other hand, Crotti reported a state of more or less constant spasticity of the stomach as shown by repeated fluoroscopic examinations.

Heimann studied the stomachs of hyperthyroid patients roentgenographically and found no gross abnormality in the gastric silhouette or emptying time. Curschmann making similar studies also found no disturbance in the form or size of the stomach. However, there was rapid gastric emptying in a few of these cases. Mueller (15) called attention to the "waterfall emptying" of the stomach and to the rapid passage of intestinal content in Basedow's disease with and without gastric symptoms.

Deutsch administered thyroid preparations intravenously to normal and to hyperthyroid individuals. He found an increase in the tonus of the colon as observed fluoroscopically. Haustral segmentation was increased as well as peristalsis.

Uermoesy and Lukacs studied the gastrointestinal passage time in a group of 24 babies before and after thyroid administration. They used carmine solution as an indicator. In 15 the passage time was shortened and in 9 lengthened. Those babies with the slowest initial time were the ones in which the passage was usually speeded.

One of the most recent and complete works on this subject is by Shirer. He studied gastrointestinal motility in a group of 42 hyperthyroid patients. Observations were made before and repeated 7 to 10 days after thyroidectomy. The patients were given a barium meal and a roentgenogram was taken 3 hours later to discover the position of the head of the barium column. If this was beyond the cecum, he considered the case one of hypermotility. On this basis, 39, or 92.8 per cent, of his patients showed hypermotility before op-



Fig. 4a.

Fig. 4. Hyperthyroid patient No. 2 (preoperative). a, This examination was made 30 minutes after giving the test meal. Barium is in the cecum at *c*. Small intestinal pattern is variable. In the jejunum in the left upper quad-



Fig. 4b.

rant the pattern is quite fine. The pattern in the ileum was "stacked coin" at *a* and patchy at *b*. b, This film made 35 minutes later shows a relative delay of barium in the ileum with a reversion toward a more normal pattern *a*.

eration. After operation the motility decreased in 76 per cent, increased in 14 per cent, and remained unchanged in 10 per cent.

#### SUBJECTS AND METHODS

The experimental group is composed of 24 patients with hyperthyroidism. The following criteria were fulfilled in selecting these subjects for study: (1) an unquestioned diagnosis of hyperthyroidism; (2) an initial basal metabolic rate of plus 30 or higher; (3) absence of associated diseases; (4) no previous treatment for the thyrotoxicosis (Exception: a few patients had received minimal iodine or roentgen therapy but not immediately preceding the study).

Twenty-three of the patients had diffuse toxic goiters and 1 had a nodular toxic goiter. In addition to the routine history, physical examination, blood count, and basal metabolic studies, the following special examinations were made: (1) serum protein deter-

minations; (2) gastric analyses; (3) roentgenological studies of the gastrointestinal tract.

The serum protein studies made on this group of hyperthyroid patients have been reported in a previous article by Brown and Mecray (9). These protein values have been used for correlation with some of our gastrointestinal data.

An oatmeal gruel mixture was used as a test meal for gastric analyses. A tube was passed and the fasting content was removed from the stomach. The test meal was then given. A specimen was collected from the stomach after one-half hour and at 15-minute intervals thereafter for a total of 6 specimens. Immediately upon collection of the first and second specimens Topfer's reagent was added to each. If no free hydrochloric acid was present in either specimen, 0.3 cubic centimeter of a 1:1000 solution of histamine acid phosphate was injected subcutaneously before the remaining samples were collected.



Fig 5 Hyperthyroid patient (preoperative) Gastric rugae are prominent. The stomach required 4 hours and 40 minutes to empty. The barium reached the cecum in 25 minutes and has progressed into the descending colon. The tone of the small intestine is not greatly increased as judged by our criteria.



Fig 6 Hyperthyroid patient No. 3 (preoperative). An orthotonic type of stomach requiring 6 hours to empty. Upper small intestines show a fine herringbone pattern. Barium reached cecum in 20 minutes and progressed through colon to fill all portions of gastrointestinal tract. Haustral markings *a* and central lumen of colon *b* are both narrow.

Roentgen studies of the gastrointestinal tract were preceded by a fast of 8 hours, usually from 12:00 o'clock midnight to the following morning. No medication was administered during this period. The patient was then given a water-barium meal and frequent fluoroscopic observations and roentgenograms were made throughout the day and often on several succeeding days. The intervals between observations were relatively short during the early hours of the study so that the gastric emptying time and the time required for the head of the barium column to reach the cecum might be accurately determined. In some cases it was necessary to make these observations every 15 minutes, in others with slower motility the interval was lengthened. However, the impossibility of keeping the patients under this strict observation for the long periods involved in determining the emptying time of

the small intestine makes these latter determinations less accurate.

In addition to time observations we have attempted a quantitative estimation of the prominence of gastric rugae, the tone and pattern of the small intestine, and the tone of the large intestine. Rugae were classified as normal, prominent, or very prominent. The intestinal tone and pattern were expressed as 1, 2, 3, or 4 plus with 0 as a hypothetical normal or base line. Since we realize that the personal equation influences such observations, we have reviewed the series repeatedly in order to check and recheck the values assigned. By so doing we believe that we have established values which are significant for comparison of the individual with the individual, the preoperative with the postoperative, and the hyperthyroid patients with the control patients.



Fig. 7a.

Fig. 7. Same case as shown in Figure 6. a, A comparison of preoperative colon studies. b, Postoperative colon



Fig. 7b.

studies. Notice the increase in width of haustral markings with what we believe is a decrease in tone after operation.

After completion of the preliminary studies the patients were prepared for operation in the usual fashion. This regimen consisted of bed rest except for 2 hours daily, sedatives, potassium iodide, with high carbohydrate high caloric intake. No vitamins were administered to this group. All the patients with diffuse toxic goiters were subjected to bilateral subtotal thyroidectomy. With few exceptions these operations were performed in one stage. The 1 patient with a nodular goiter required only a hemithyroidectomy. At intervals from 3 to 12 months after operation follow-up studies were made. In 1 case only was there any clinical or basal metabolic evidence of persistence of the thyrotoxicosis. At the time of the follow-up visit roentgen studies of the gastrointestinal tract were repeated exactly as they had been made before operation.

Finally, a control group of 14 composed largely of medical students, doctors, and nurses was subjected to similar roentgeno-

logical studies of the stomach and intestines. Individuals were selected who had no gastrointestinal complaints and who had no signs or symptoms to suggest thyroid dysfunction.

#### EXPERIMENTAL FINDINGS

*Gastric secretion.* In Table I are presented the data obtained from the gastric analyses in our group of hyperthyroid patients. This material has been analyzed only in respect to achlorhydria. Although the figures for free and total acid are available for all cases studied, we have felt that further to subdivide the group with acid into those with low, normal, or high figures would merely add confusion. Such a subdivision would immediately stimulate arguments as to the normal range of free and total acid, the influence of histamine on such figures, etc.—discussion which we do not propose to consider in this presentation.

However, we wish to make clear our interpretation and usage of the word achlorhydria.

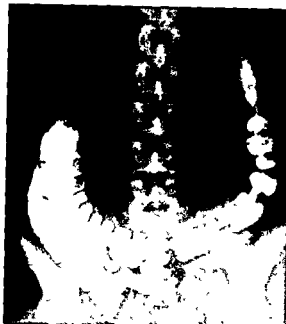


Fig 8a

Fig 8 a, Control case 1. Colon of a normal individual which also fits our arbitrary normal as to tone. For comparison with b. b, Hyperthyroid patient, No. 2 (preoperative). This colon has been regarded as hypertonic (2 plus).



Fig 8b

Note the narrow haustral markings at b, c, and d. The lumen of the colon between the haustra is also somewhat narrowed in comparison with that of the control patient in a.

Achlorhydria means that under certain given experimental conditions an aspirated sample of gastric content contained no titratable free acid. This may have been the result of the suppressed hydrochloric acid secretion but not necessarily so. Hypersecretion of mucus, regurgitation of duodenal content, swallowing of an excess of saliva, or the buffering action of ingested substances, one or all may depress free gastric acid. Much of the gastric analysis work in the literature is meaningless because these facts have not been appreciated.

Thirteen, or 50 per cent, of 26 patients showed no free acid without histamine. Lerman, Pierce, and Brogan (30) found only 13 per cent achlorhydria in a series of 200 normal individuals studied by them. They used an alcohol test meal with histamine. Keefer and Bloomfield reported 1500 consecutive gastric analyses using the Ewald test meal. In those without organic disease anacidity was present in 14.5 per cent. The increased incidence of achlorhydria in our hyperthyroid group as

compared to these normals can hardly be questioned even though the technique for gastric analysis was slightly different in each instance.

Unlike many of those whose works have been reviewed, we have not been able to demonstrate a significant relationship between the incidence of achlorhydria and basal metabolic rate, hemoglobin percentage, duration of symptoms, or serum protein level. The age and sex differences are approximately those reported for normal groups. Vanzant and co-workers found in a series of 3,381 normal individuals a greater tendency to achlorhydria in women than men and a definite increase in the incidence of anacidity with increase in age. Lerman, Pierce, and Brogan (30) report an incidence of achlorhydria of 3.6 per cent in those under 30 and of 24.4 per cent in those from 55 to 64 years of age.

*Gastrointestinal motor activity.* In spite of our review of the literature on the subject, we entered upon this study with few preconceived notions as to what fundamental gastrointesti-

changes were to be found in hyperthyroidism. It was, therefore, necessary to outline in advance an all inclusive list of fluoroscopic and roentgenographic observations to be made on each individual studied. For convenience in presentation and analysis this material has been divided into the following groups: (1) type of stomach, tone of stomach, gastric rugae, gastric movements, (2) time stomach started to empty; (3) time stomach was completely empty (gastric emptying time); (4) small intestinal tone and pattern; (5) time barium reached the cecum; (6) time small intestine was completely empty (small intestinal emptying time); (7) tone of colon; (8) time colon was empty (motility of colon).

1. *Type of stomach, tone of stomach, gastric rugae, gastric movements.* The orthotonic type of stomach was found in all individuals studied, both in the hyperthyroid and control groups. It was a J shaped organ which in erect posture, with the test meal used (5 ounces of barium and 5 ounces of water), showed no tendency for any of its walls to collapse. The transverse diameter of the upper third of the stomach (junction of the fundus and the body) and the transverse diameter of the lower third (junction of the body and pyloric antrum) were approximately the same (Figs. 1a and 3), except when the stomach was very long.

We believe that the type of stomach is determined by anatomical factors, both intrinsic and extrinsic, and do not regard it as an expression of the physiological tone of the organ.

The evaluation of gastric tone in each case has been based upon the manner in which the stomach accepted the first few swallows of the test meal. When the barium progressed in an uninterrupted and regular manner from the esophagus to the pyloric antrum in about 10 seconds, tone was considered normal. In those stomachs which were classified as hypertonc, the swallowed barium was held in the fundus for varying lengths of time and then traveled very slowly toward the antrum. One must be extremely careful not to include in the hypertonic group a cascade type of stomach in which the barium may be trapped in the fundus.

TABLE I.—GASTRIC ANALYSES IN HYPERTHYROID CASES

	No Free HCl—9 cases	Free HCl—17 cases
	+65	+61
Average basal metabolic rate..	79	79
Average hemoglobin (Sahli) per cent.....	42	33
Average age—years.....	2 (25%)	6 (75%)
Sex—	7 (39%)	11 (61%)
Males.....		18.3
Females.....	15.2	
Average duration of symptoms—mos.....		6.16
Average serum protein—grams per cent.....	6.15	

There were originally 26 patients in our experimental hyperthyroid group. All were studied by gastric analysis. However, 2 of the patients failed to complete their postoperative roentgenograms; thus the group was reduced to 24 for the studies on gastrointestinal motor activity.

The stomach was regarded as hypotonic when the barium traveled faster than normal from the fundus to the antrum. Occasionally the barium moved as though falling through space. Observations on gastric tone were always made before palpation of the abdomen was instituted.

Data were compiled classifying the stomachs of the hyperthyroid patients as to type and tone. Illustrating the point already made that the type of stomach is not a function of its tone, we note that there often was a difference between preoperative and postoperative tone, in any given case, while the type remained the same through the study. On comparing the postoperative with the preoperative it is seen that the change in tone was predominantly downward with a decrease in 10 cases, an increase in 5, and with the remainder of the group unchanged or undetermined. The same data was compiled for the controls. Again the orthotonic type of stomach was found throughout the group. Gastric tone was normal in 9 cases, in 2 the stomach was hypertonic, in 2 hypotonic. Unfortunately, when derived from a sample of this size, the differences in tone observed when the preoperative group is compared with the postoperative group or with the controls are not of sufficient magnitude to be of significance (Methods I and III).<sup>1</sup>

The significance of the prominence of gastric rugae as determined by roentgen examination has not been fully established. In many in-

<sup>1</sup>See appendix for definition of significance and for brief description of methodology. The method number in parenthesis throughout the presentation refers to the corresponding method in the appendix.



TABLE II.—TIME STOMACH STARTED TO EMPTY

Controls		Hyperthyroid cases		Direction of change
	Time—minutes	Preoperative time—minutes	Postoperative time—minutes	
A	*3	1 *2	*2	Unchanged
B	*2	2 *2	*6	Increased
C	3+	3 *4	Not immediately	?
D	*2	4 *2	*3	Increased
E	*3	5 *9	2+	?
F	5+	6 *5	2+	?
G	*5	7 Almost immediately	*7	Increased
H	*1	8 *Immediately	*3	Increased
I	*3	9 Slight delay	Slight delay	Unchanged
J	*Immediately	10 4+	*12	?
K	*7	11 Delay	3+	?
M	*7	12 Delay	*15	?
N	*5	13 Slight delay	*5	?
O	*5	14 Delay	*5	?
		15 *1	*Immediately	Decreased
		16 4+	23+	?
		17 *2	*4	Increased
		18 *3	*4	Increased
		19 *1	*3	Increased
		20 *5	*3	Decreased
		21 *3	4+	Increased
		22 Almost immediately	*2	Increased
		23 *Immediately	*2	Increased
		24 *2	*9	Increased
Total 43 (22 cases)*		41 (25 cases)*	85 (17 cases)*	
Mean 3.58		7.73	5.00	
Range 0—7		0—9	0—15	

NOTE.—Means are only for cases in which time is accurately recorded. Pluses represent an undetermined length of time to be added to the time recorded.

stances increase in prominence may be due to the hypertrophic inflammatory changes of gastritis. In some cases hypertrophy and edema behind pyloric obstruction may explain the picture. In other cases the prominence of mucosal folds may be purely passive and secondary to an increase in gastric tone with contraction of the underlying muscular coats.

Without further explanation of their significance, we present our observations on gastric rugae. The rugae have been described as normal, prominent, or very prominent (Figs. 1a and 3). By a comparison of preoperative

studies on the hyperthyroid group with the postoperative studies, it is seen that gastric rugae were less prominent after operation in 11 of the 12 cases which showed a change. The statistical significance (Method I) of these findings is somewhat offset by the fact that 12, or 50 per cent, of the cases showed no change in rugae. Although gastric rugae were definitely less prominent in the patients after operations than before, they were still significantly more prominent than in the controls (Method III). Perhaps we are dealing with a persistent hyperthyroid effect similar to that reported for dogs by Kratinoff and Fetter and Carlson (20).

Although gastric movements were carefully studied under the fluoroscope in all cases of hyperthyroidism, both before and after operation, and in the controls, no significant or uniform differences in type, frequency, or depth of peristaltic movements were found.

2. *Time stomach started to empty.* It has been the experience of one of us (Pendergrass) that the rapidity with which the stomach starts to empty, as determined fluoroscopically, varies greatly from individual to individual and from time to time in the same individual. This is equally true of subjects with or without gastrointestinal pathology. Uncontrollable psychic influences incident to the start of a study, often strange and formidable to the patient, probably have considerable effect on these short time observations. The same is not true of the observations on gastric emptying time, time for the barium to reach the cecum, etc.—observations which extended over a relatively long period of time and upon which the effect of such transient influences becomes minimal.

Because of these considerations we must not overstress the importance of the data presented in this section. Observations on the rapidity with which the stomach started to empty once the barium had reached the pyloric antrum are presented in Table II. In 15 of the hyperthyroid group these observations are accurate enough for comparison of preoperative and postoperative times. In 11 of these 15 cases gastric emptying was initiated more slowly after operation. A comparison of mean times (preoperative 2.73 minutes with

postoperative 5.00 minutes) adds to the significance of the directional change. However, neither the preoperative nor the postoperative mean varies significantly from the control mean (Methods I, III, and IV).

3. *Time stomach was completely empty.* The gastric emptying time has been determined for all cases studied. Frequency of roentgenological observations has been governed in part by a desire to record as accurately as possible the time necessary for the stomach to empty itself completely of the barium meal. In most instances it has been impossible both from the standpoint of x-ray exposure and time consumed to observe the actual endpoint in gastric emptying. Especially was this true when the emptying time was greatly prolonged. The gastric emptying time was then determined by interpolating between observations made on either side of the true endpoint. We have estimated our maximum error by this method as 30 minutes. The error for the majority of cases was considerably less than this maximum.

The material on gastric emptying time is presented in Table III. Attention must be called to the 3 preoperative hyperthyroid patients whose stomachs were not completely empty at the end of this first day's period of observation. The undetermined additional time required for gastric emptying in these cases is represented by plus signs. These plus signs have been disregarded in our subsequent calculations for the sake of simplicity. This is justifiable since to include them would serve only to increase further the magnitude of the changes which the data demonstrate.

Preoperative and postoperative "gastric emptying times" have been compared for each individual of the hyperthyroid group. Changes of less than 30 minutes were regarded as insignificant because they did not exceed the estimated maximum error of our observations. In 16 cases the stomach emptied more rapidly after operation. In 5 cases the time was unchanged, and in the 3 remaining the stomach emptied more slowly. The significance of this group change toward more rapid gastric emptying can scarcely be questioned (Method I).

Having established this definite directional change we were interested next in studying

TABLE III.—GASTRIC EMPTYING TIME

Controls		Hyperthyroid Cases		Direction of change
	Time—minutes	Preoperative time—minutes	Postoperative time—minutes	
A	120	1 120	70	Decreased
B	210	2 180	285	Increased
C	150	3 360	330	Decreased
D	156	4 120	180	Increased
E	120	5 360	375	Unchanged
F	120	6 330	186	Decreased
G	170	7 315	123	Decreased
H	08	8 210	160	Decreased
I	160	9 160	165	Unchanged
J	185	10 150	240	Increased
K	138	11 260	240	Unchanged
M	120	12 450+	210	Decreased
N	140	13 360+	120	Decreased
O	120	14 133	137	Unchanged
		15 240	90	Decreased
		16 360+	240	Decreased
		17 420	180	Decreased
		18 160	105	Decreased
		19 120	65	Decreased
		20 210	120	Decreased
		21 320	120	Decreased
		22 200	135	Decreased
		23 150	165	Unchanged
		24 280	130	Decreased
Mean	143.36	247.83	175.04	

the magnitude of these observed differences. Groups were compared by using mean values for the gastric emptying times. On an average the stomach took 73 minutes longer to empty in the preoperative hyperthyroid patients than in the postoperative, and 104 minutes longer in the preoperative than in the controls. Both differences are significant (Methods III and IV). This is not true of the difference between the postoperative patients and the controls which was only 32 minutes. The postoperative reversion toward normal in the case of the gastric emptying time was much more complete than for gastric rugae.

Finally, gastric emptying times were analyzed as to variance. A very highly significant difference was found when preoperative hy-

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perthyroid patients were compared with controls (Method V). That thyrotoxicosis should produce a varying rather than a uniform delay in gastric emptying, as individual cases are compared, is to be expected in the light of similar and better known effects on other organs. In a group of hyperthyroid patients with approximately the same basal metabolic rate, individual variations in pulse rate, degree of weight loss, severity of eye signs, tremor, etc., are the rule. Why this wider variation persisted after operation in the hyperthyroid group when the mean value for gastric emptying time so closely approached the control value is a question for which we have not found a satisfactory answer.

4 *Small intestinal tone and pattern.* Perhaps the most striking change noted in this study of the gastrointestinal tract in hyperthyroid patients and at the same time the most difficult to evaluate quantitatively were those in small intestinal tone and pattern. It has already been explained that we have chosen to express the degree of change as 1, 2, 3, or 4 plus as compared with an arbitrarily chosen normal. This has been necessary for convenience in analysis and correlation with our quantitative data.

Ordinarily the jejunal loops, as demonstrated roentgenographically, are located in the upper and lower quadrants on the left side. In many of our hyperthyroid patients the jejunal loops occupied a midline position and were transversely placed (Fig. 1). We have interpreted these changes as indicative of small intestinal shortening and believe that this shortening may explain in part the increase in small intestinal motility (5, Time to

The interpretation of hypertonicity in the small intestine was based upon the apparent decrease in the lumen or transverse diameter of the gut and the types of pattern observed.

Ordinarily (under normal circumstances) there occurs a coarse herringbone pattern in the upper small intestine. In the hyperthyroid patients the pattern was finer and in many instances the herringbone was replaced by an "iron filing" type of pattern (Figs. 1b and c, 6). These changes often were not uniform throughout the entire length of small intestine,

and there was occasionally a relative delay of barium in the distal ileum with a reversion toward a more normal pattern (Fig. 4b).

There were no outstanding abnormalities of small intestinal movements noted during the repeated fluoroscopic examinations. Occasional peristaltic rushes were observed and segmentation was often well demonstrated but with no greater frequency than in the controls.

Data were compiled also on small intestinal tone and pattern. A comparison of the hyperthyroid groups shows that after operation there was a predominant change in the direction of decreased tone with a reversion of the pattern toward normal (Fig. 2).

The degree of change is expressed by a difference in means for the groups, computed in terms of pluses. The differences between the preoperative mean and that of the control group may be accepted as highly significant (Methods I, III, and IV). As in the case of gastric rugae, however, the postoperative approach to the control level was not complete.

5 *Time to cecum.* An expression of small intestinal motility, time to cecum is defined as the time elapsing from administration of the meal until the head of the column of barium reached the large intestine. As in determining gastric emptying time, it was seldom possible actually to observe the true end point. Again it was necessary to estimate it by interpolating, in this instance, between observations made before and after the opaque meal entered the cecum. Because of the relatively short times involved, estimations of time to cecum could be made with much greater accuracy than those for gastric emptying time. Our maximum error for time to cecum probably did not exceed 10 minutes.

Data assembled showed that after operation 18 of the 24 hyperthyroid patients required increased time for the barium to reach the cecum. In 2 other cases the postoperative change was in the same direction but did not exceed our estimated maximum error of 10 minutes. In only 4 instances was the time to cecum decreased after operation.

As in many of the preceding sections a significant directional change (Method I) is substantiated by the degree of change determined

by comparison of means. The difference of 40 minutes between the preoperative and postoperative hyperthyroid means and the difference of 60 minutes between the preoperative hyperthyroid mean and that of the controls are both highly significant in themselves. That the postoperative return to normal has been fairly complete is shown by the relatively insignificant difference between the means for this group and the control mean (Methods III and IV).

6. *Time small intestine was completely empty (small intestinal emptying time).* Because of the long periods involved, determination of the time required for the small intestine to empty is in many cases an approximation. Frequently some of the barium still remained in the small intestine at the end of the first day. In 9 of the hyperthyroid cases a comparison of the preoperative and postoperative small intestinal emptying times was impossible. In 5 instances there was no change. In 4 individuals the small intestinal emptying time decreased, and in 6 it increased after operation. This failure to demonstrate a definite change for the group as a whole is not unexpected when we consider that the postoperative decrease in gastric emptying time and the increase in time to cecum tended to balance one another.

The means for the preoperative and postoperative hyperthyroid groups and for the controls have been computed; only those cases were used whose small intestinal emptying times were accurately determined. These means obviously do not differ significantly.

7. *Tone of colon.* Adopting an arbitrary normal or 0, we have expressed hypertonicity of the large intestine in terms of pluses. The transverse diameter of the colon and the number of haustral markings vary in different patients and even in the same patient, at different intervals. Standards of normalcy are difficult to establish and describe. In our experience, and for the purpose of this study, the colon shown in Figure 8a may be regarded as normal. Its lumen measures about 5 centimeters in diameter and haustral markings are quite wide. Narrowing of the lumen and haustral markings was interpreted as evidence of increased colonic tone (Figs. 7a and 8b).

In the preoperative hyperthyroid patients the tone of the large intestine was definitely greater than that of the controls. After operation 13 of the hyperthyroid cases showed a decrease in tone and 2 an increase. In 5 instances the tone of the colon remained essentially unchanged, and in 4 no comparison was possible. In spite of this decrease, the colonic tone of the postoperative hyperthyroid group remained slightly greater than that of the control group. The significance of these differences is established by Methods I, III, and IV.

8. *Time colon was empty (motility of colon).* Final observations dealt with the motility of the large intestine. Following the first day's studies, daily roentgen examinations were made in order to determine in which of the succeeding 24 hour periods the evacuation of the barium from the colon was completed. Although far from ideal, this method of expressing motility was more satisfactory than our concomitant attempt to record the time and number of barium-containing bowel movements. In the preoperative hyperthyroid group, 14 of 20 cases emptied their colons of barium in less than 48 hours. In none of the controls was this true. After operation the colonic emptying time of the hyperthyroid patients had increased in 11 cases and remained the same in 5. In the remaining cases an accurate comparison could not be made. This postoperative reversion of the hyperthyroid group toward the control normal for large intestinal motility is both striking and significant (Method II).

As compared to the controls, the hyperthyroid group showed preoperatively the following differences: (1) an increased incidence of achlorhydria; (2) increased prominence of gastric rugae; (3) an increase in the rapidity with which the stomach started to empty; (4) a delay in gastric emptying (increased gastric emptying time); (5) increased small intestinal tone with an abnormal pattern; (6) increased small intestinal motility (decreased time to cecum); (7) increased large intestinal tone; (8) increased large intestinal motility.

After operation, the hyperthyroid cases more closely resembled that of the controls. In many instances differences had entirely dis-

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TABLE IV

	Gastric rugae* Means	Gastric emptying time min Means	Small intestinal tone and pattern Means	Time to ocum min Means
1 Age < 36½ yrs	2 267	246 0	2 750+½	55 4
> 36½ yrs	2 083	248 0	2 938+½(S)	91 2
2 Sex Males	2 125	237 5	2 635+½	94 6
Females	2 135	253 0	2 710+½(S)	62 6
3 Pulse rate < 103	2 700	298 3	2 500+½	67 1
> 103	2 410(S)	283 2(S)	2 850+½	77 6
4 Duration symptoms < 7 mos	2 400	270 5	2 400+½	89 5
> 7 mos	2 090	230 2	2 346+½	63 7
5 Percent wt loss < 15% lbs	2 333	247 2	2 750+½	68 8
> 15% lbs	2 917	248 6	2 958+½(S)	77 7
6 B V R < +60	2 800	205 0	2 600+½	74 6
> +60	2 357	278 4	2 179+½	72 3
7 Hemoglobin < 8.1	2 545	280 4	2 777+½	75 6
8.1 or more	2 750(S)	273 2	2 023+½(S)	71 2
8 Achlorhydria %	2 000	281 2	2 500+½	71 4
No	2 188	250 3	2 282+½	74 2
9 Serum protein < 6.0 g/l	2 250	242 5	2 125+½	66 4
> 6.0 g/l	2 000	253 2	2 583+½	85 1
10 Nausea and vomiting Yes	2 600	294 6	2 700+½	70 0
No	2 263	261 8	2 305+½	74 1
11 Appetite increase Yes	2 267	266 7	2 400+½	70 5
No	2 380	216 4	2 278+½	77 8
12 Indigestion Yes	2 143	279 0	2 420+½	54 6
No	2 118	235 0	2 324+½	80 9
13 Bowel habits Constipation	2 750	245 8	2 500+½	43 8
Diarrhea	2 500	274 2	2 500+½	79 1

\*Values assigned: Normal—1, Prominent—2, Very Prominent—3.  
 †The median value of all hyperthyroid cases.  
 (S) Difference in means is significant.

appeared. Generally speaking, the changes toward normal with respect to motility were more complete than the changes in tone or pattern.

Several factors were studied for a possible relationship to the gastrointestinal variations

observed in the preoperative hyperthyroid patients. Considerations governing the selection of these factors for analysis were numerous. The hyperthyroid and control groups differed somewhat in age and sex distribution. So it was necessary to investigate the possibility of a casual relationship between these two factors and the gastrointestinal differences.

Attempts were made to correlate the gastrointestinal variations with the effects of the thyrotoxicosis on other organs or systems of the body and with the basal metabolic rate and duration of the disease. Finally we tried to explain the gastrointestinal symptoms presented by our hyperthyroid patients on the basis of the underlying changes in physiology as determined by our roentgen studies. Table IV are presented the results of our investigations with respect to prominence of gastric rugae, gastric emptying time, small intestinal tone and pattern, and time to defecum. We were not able to discover any one constant relationship to all of the gastrointestinal variations studied. Only in isolated instances was there evidence of correlation. These will be discussed briefly.

**Age.** Age apparently had little influence on the phases of gastrointestinal activity under investigation with one possible exception. Small intestinal tone was greater and the pattern was more abnormal in the hyperthyroid subgroup below the median age. However, an increase rather than detract from the significance of the differences observed in small intestinal tone and pattern when the hyperthyroid patients were compared with the younger controls.

**Hemoglobin level and pulse rate.** The hemoglobin level apparently bore a significant relationship to prominence of gastric rugae and to small intestinal tone and pattern. The rugae were more prominent and the small intestinal tone was greater in the subgroup with hemoglobin values below the median. Pulse rate was correlated with gastric rugae and gastric emptying time. The rugae were more prominent and the stomach emptied more slowly in the subgroup with pulse rates above the median.

*Sex and weight loss.* Two other isolated relationships were noted. The small intestinal tone and pattern showed greater alteration in female hyperthyroid patients than in males and also in those individuals whose weight loss was above the median as compared to those below.

*Achlorhydria and serum protein level.* Two negative findings merit special attention. One is the lack of correlation between achlorhydria and gastric emptying time. Established teaching postulates a more rapid gastric emptying in the presence of achlorhydria. Bockus, Bank, and Willard found this true in 87 or 41.4 per cent of 210 cases of achlorhydria studied by them. Either this effect of achlorhydria was absent in our cases or the factor or factors which increase gastric emptying time in hyperthyroid patients have more than compensated for this tendency to rapid emptying.

The influence of the serum protein level upon certain phases of gastric and intestinal motility has been demonstrated both in the experimental animal and in various pathological states in humans (2, 3, 36). However, there was a complete lack of correlation between the slightly altered serum protein values and the gastrointestinal variations in our hyperthyroid patients.

*Vitamin B complex deficiency.* One factor which may have played an etiological rôle in the production of the gastrointestinal abnormalities observed in our hyperthyroid patients is a vitamin B complex deficiency. Cowgill has shown that the vitamin B requirement of man is greatly increased by elevations in metabolic rate, and there is much accumulated evidence (17, 21, 43) pointing to an actual deficiency in this vitamin in many cases of hyperthyroidism.

The effect of a B complex deficiency on gastric emptying and small intestinal motility has been studied roentgenologically by Heublein, Thompson, and Scully. Dogs were used as experimental animals. A B complex deficiency caused marked delay in gastric emptying similar to that observed in our hyperthyroid patients. Although the vitamin deficient dogs showed a moderate delay in small intestinal motility, the most consistent abnormality in the small intestinal pattern was that of diminished bowel caliber with hypertonic appearance. This, too, is comparable to the picture in our hyperthyroid group.

If we are justified in comparing these roentgenological observations in the experimental animal with those in our human subjects, the proposed etiological relationship between B complex deficiency and the gastrointestinal abnormalities observed in our hyperthyroid patients is supported by the similarity of these findings.

Scatter diagrams 1 to 13 were prepared in our search for interrelations between the various gastrointestinal observations themselves. No significant correlations were found either visually or by computing the measures themselves (Methods VI and VII).

Failure to establish interrelations between the various gastrointestinal abnormalities found in our hyperthyroid patients does not necessarily detract from the significance of our observations. In comparison with the controls the hyperthyroid patients as a group showed a delay in gastric emptying and an increase in small intestinal motility. It does not follow, however, that the hyperthyroid individual with the longest gastric emptying time must have the shortest time to cecum or vice versa; especially since this relationship cannot be demonstrated within the control group itself.

Neither does the lack of correlation between the gastrointestinal abnormalities and the other signs and symptoms of hyperthyroidism argue against a common etiological factor. Hyperthyroidism is a disease noted for its "dispersion phenomena" (44), that is, for the variable intensity of its effects on the different organs or systems of the body. In any given case of thyrotoxicosis one sign or symptom, or even a group of symptoms, may dominate the clinical picture and bear no relationship to the severity of the other manifestations of the disease.

#### SUMMARY AND CONCLUSIONS

We have studied the gastrointestinal tract in 24 hyperthyroid patients and 14 normal controls. Differences between the two groups have been noted and subjected to careful

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statistical analysis in order to establish their significance. As a result of these studies we feel justified in concluding that the following gastrointestinal changes are characteristic of hyperthyroidism:

1. An increased incidence of achlorhydria.
2. Increased prominence of gastric rugae.
3. An increase in the rapidity with which the stomach starts to empty (of questionable significance).
4. A delay in gastric emptying (increased gastric emptying time).
5. Increased small intestinal tone with an abnormal pattern.
6. Increased small intestinal motility (decreased time to cecum).
7. Increased large intestinal tone.
8. Increased large intestinal motility.

## APPENDIX

**A Definition of degrees of significance** Two types of differences have been encountered in the statistical study, (a) the difference between an actual finding and a hypothetical value, and (b) the difference between the actual findings in two groups. In each instance, however, the statistical problem is to test the permissibility of the hypothesis that there is no difference between the actual involved. The solution of this problem requires the determination of the probability of obtaining a difference as great or greater than the one actually occurring if chance alone had operated. The definitions of the varying degrees of significance used throughout this study are related to this probability in the following way

Probability	Degree of significance
1 Greater than 0.05	Not significant
2 0.05 to 0.01 exclusive	Significant
3 0.01 or less	Highly significant
4 0.001 or less (rarely determinable from prepared tables)	Very highly significant

**B Methodology** Various methods have been used in the statistical analysis of the data. These may be explained in brief as follows

**Method I** Determining the significance of the difference between an observed and a hypothetical ratio  
Let  $p$  be the observed ratio and  $q$  the expected events to the number of cases  
Let  $q = 1 - p$   
The binomial,  $(p+q)^n$ , was then expanded and the desired probabilities were determined exactly, because the successive terms of the expansion give the probabilities that (1)  $\frac{n-1}{n}$  (2)  $\frac{n-2}{n}$  etc., events will actually be obtained if chance alone operated.  
(3)  $\frac{n-3}{n}$  etc.

**Method II** Determining the significance of the difference between two observed percentages  
Let  $p_1$  = the observed ratio in the preoperative group  
Let  $p_2$  = the observed ratio in the postoperative group  
Let  $q_1 = 1 - p_1$

Let  $n_1 = 1 - p_1$   
Let  $n_2$  = number of determined cases in preoperative group  
Let  $n_3$  = number of determined cases in postoperative group  
Let  $p_1 + p_2 = \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2}$   
Then  $SE(p_1 - p_2)$  (the standard error of  $p_1 - p_2$ ) =  $\sqrt{p_1 + p_2 \cdot q_1 + \frac{n_1 + n_2}{n_1 n_2}}$  and the probability may be determined from prepared tables for the ratio  $\frac{p_1 - p_2}{SE(p_1 - p_2)}$

(See Croxton and Cowden *Applied General Statistics*, p. 358, 359, New York: Prentice Hall, Inc.)

**Method III** Determining the significance of the difference between the means of two groups  $t$ -test  
(See R. A. Fisher's *Statistical Methods for Research Workers*, 6th ed., p. 130 London Oliver and Boyd, 1936)

**Method IV** Determining the significance of the mean difference of paired items:  $t$ -test (R. A. Fisher, op cit, p. 126, example 19).

**Method V** Determining the significance of the difference of the variability of two groups:  $z$ -test (See Croxton and Cowden, op cit, pp. 344-348).

**Method VI** Determining the significance of the difference of the Pearsonian coefficient of correlation from zero  $t$ -test (See Croxton and Cowden, op cit, pp. 681, 682)

**Method VII** Determining the rank difference coefficient of correlation (See Croxton and Cowden, op cit, pp. 685, 686).

Professor Burton R. Camp of Wesleyan University has made helpful suggestions concerning the statistical analysis

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# SMOOTH MUSCLE TUMORS OF THE GASTROINTESTINAL TRACT AND RETROPERITONEAL TISSUES

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**I**N recent years a number of very interesting benign and malignant leiomyomas of the gastrointestinal tract have been observed at the Presbyterian Hospital and in the laboratory of Surgical Pathology of Columbia University, and the striking characteristics exhibited by a few of these have stimulated a study of all neoplasms of this classification available in the hospital and laboratory records. To complete this investigation, a comprehensive analysis of the literature was undertaken and it was hoped that such a review might reveal a definite pattern for these tumors. More than 400 publications were examined and such confusion was found that reliable detailed statistics could not possibly be computed, but correlation of the substance of this material with the conclusions drawn from the series of cases at hand makes it possible to offer several basic general principles, which, it is hoped, will be of value diagnostically and therapeutically.

Seldom does this type of gastrointestinal tumor receive the benefits of more than a brief paragraph or two in the standard textbooks and this is truly incomprehensible when the mass of literature is considered. Because of this undeserved obscurity the correct proper diagnosis is seldom made, and the treatment instituted has not always been the most desirable one. The present study has been undertaken with the hope of clarifying our knowledge concerning these tumors.

During the 26½ year period from October, 1913 to May, 1940, 60 smooth muscle tumors of the gastrointestinal tract and retroperitoneal regions have been studied (Table I)—56 came from the Presbyterian Hospital and 4 came from other sources. Thirty of these caused clinical symptoms and all but 8 were treated by surgical removal. Four retroperitoneal tumors were removed by the College of Physicians and Surgeons, Columbia University and the Department of Surgery, Presbyterian Hospital, New York.

tonal tumors were subjected to biopsy only, 1 was treated with roentgenotherapy, and in 1 gastric and 2 duodenal cases patients were not operated upon because of a failure to make the diagnosis. The rest were all small intramural tumors, 7 of which were found by chance at operation (Table II), and 23 were incidental findings at autopsy (Table III). This makes an incidence of 0.39 per cent of our autopsy population. Rieniets (1930) reported an incidence of 16 per cent in 200 consecutive autopsies performed at the Mayo Clinic.

Our investigation is concerned especially with those tumors which caused symptoms; a total of 30 cases (Table IV). These were distributed as follows: stomach, 8; duodenum, 2; jejunum, 1; ileum, 3; Meckel's diverticulum, 1; colon, 2; rectum, 5; retroperitoneal, 8.

After prolonged study we have tentatively concluded that 21 of them should be classified as malignant and 9 as benign. All of the smooth muscle tumors found by chance were considered benign, which gives 65 per cent benign and 35 per cent malignant in the whole group. For reasons which will presently appear, we do not feel at all confident that this division is accurate and above criticism, and we have therefore been uncertain about the question of nomenclature. Ghon and Hintz (1909) suggested that the term malignant leiomyoma be used instead of leiomyosarcoma and this is approved by Clerici Bagozzi (1934), As will be shown, one can never be entirely certain that any leiomyoma is necessarily benign, except the small intramural tumors which are chance findings at autopsy or operation. Any of the tumors large enough to cause clinical symptoms may kill by infiltrative growth or occasionally by metastasis, although as a matter of record very few of them are reported to have done so. The following are indebted to Dr. J. W. Jobling, professor of pathology at Columbia University, for permission to include these and other clinical cases which came to autopsy.

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TABLE I.—DISTRIBUTION AND CLASSIFICATION OF 60 SMOOTH MUSCLE TUMORS

Site	Cases	Clinical	Incidental at operation	Incidental at autopsy	Malignant	Metastases	Recurrence
Stomach	33	8	5	20	5	2	0
Duodenum	3	2	0	1	1	1	0
Jejunum	1	1	0	0	2	0	0
Ileum	5	3	0	0	1	0	0
Meckel's diverticulum	1	1	0	0	1	0	0
Colon (left)	3	2	1	0	0	4	1
Rectum	5	5	0	0	6	3	1
Retroperitoneal	9	8	1	0	21	6*	3**
Total	60	30	7	23	21	6*	3**

\*29% of 21 malignant leiomyomas, 19% of 30 clinical leiomyomas.  
 \*\*14.5% of 21 malignant leiomyomas, 9.5% of 30 clinical leiomyomas.

them do so. There is no basic objection to the use of leiomyosarcoma instead of malignant leiomyoma, for in both instances the term connotes a malignant smooth muscle tumor. But in the minds of many the word "sarcoma" suggests a high degree of malignancy and, as we shall show, the malignant smooth muscle tumors as a group do not justify this reputation. For this reason, we favor the use of "malignant leiomyoma" for those tumors which exhibit histological or clinical evidences of malignancy.

The *etiological factors* involved remain entirely speculative and range from theories concerned with congenital anlage (Cohnheim-Ribbert) to suggestions that these tumors result from inflammatory stimulation of smooth muscle tissue (Virchow). It is not possible, therefore, to state definitely anything more than the fact that these tumors originate in the muscularis of the gastrointestinal tract. Rarely, the site of origin is the muscularis mucosae (Fig. 26), and it is further conceivable that the vascular musculature may give rise to a leiomyoma.

There is no demonstrable difference in incidence based on sex, race, or geography. In general, 60 per cent occur between 40 and 60 years, while 20 per cent are under 40 and 20 per cent over 60. The average age approximates 47 and the youngest patient was a 2 year old African male child (Kroeber, 1934), while the oldest was an 81 year old male

TABLE II.—7 INCIDENTAL LEIOMYOMAS FOUND AT OPERATION

Case	Sex Age	Operation	Site	Size
31	F 63	Colostomy and perineal proctectomy for carcinoma of rectum. Excision of leiomyomas	Stomach and right ovary	Each—2 cm.
32	M 54	Subtotal gastric resection for gastric ulcer	Stomach	3 by 2 mm.
33	F 61	Subtotal gastric resection for gastric ulcer	Stomach	7 mm.
34	M 66	Subtotal gastric resection for carcinoma	Stomach	7 by 3 mm.
35	M 42	Excision of hypernephroma of left kidney. Excision of leiomyoma	Stomach	2 by 1.5 by 1.5 cm.
36	M 57	Abdominoperineal resection for carcinoma of rectum	Sigmoid colon	1.5 by 1.5 cm.
37	M 65	Appendectomy and excision of leiomyoma	Omentum	4 mm

(Ghon and Hintz, 1909). By far the commonest reported site of occurrence is the stomach, with a total of 629 cases (61.5 per cent). Then, in order of frequency, are the following: small intestine, including appendix and Meckel's diverticulum—197 cases, 19 per cent; rectum—69 cases, 7 per cent; duodenum—51 cases, 5 per cent; retroperitoneal tissue, including omentum and mesenteries—43 cases, 4.5 per cent; and colon—29 cases, 3 per cent; a total of 1,018 cases. It is safe to assume that many more have been unreported, unrecognized, or incorrectly diagnosed.

In general, 60 per cent of the gastric tumors occur in the pyloric region, 25 per cent in the pars media, and 15 per cent in the cardia. They exhibit a predilection for the curvatures, with the lesser more frequent in the ratio of 3 to 2, and twice as many are found on the posterior as on the anterior surface.

In the small intestine, 80 per cent occur with equal frequency in the ileum and jejunum, while 20 per cent are found in the duodenum. Rarely, the appendix or a Meckel's diverticulum is the site of origin.

In the large bowel, 83 per cent arise in the rectum and 17 per cent in the colon. Of the latter, almost 50 per cent occur in the cecum.

## PATHOLOGY

In the gastrointestinal tract both benign and malignant tumors are firm, occasionally indurated, well defined, rounded, or lobulated

TABLE III.—23 INCIDENTAL LEIOMYOMAS FOUND AT AUTOPSY\*

Case	Autopsy	Sex Age	Site	Size
1	8325	M 66	Stomach	4 mm
2	8477	M 75	Stomach (2)	3.5 by 3.25 cm. & 2 mm
3	9160	M 53	Stomach (2)	Largest—6 mm
4	9565	M 65	Stomach	4 by 3 mm
5	9846	F 53	Stomach	7 mm
6	9930	M 63	Stomach	3 mm
7	9949	M 60	Stomach	6 mm
8	9988	M 58	Stomach	6 by 4 mm
9	10144	F 57	Stomach	3 mm
10	10931	F 57	Stomach (2)	Each—7 mm
11	21453	F 69	Stomach and left broad ligament	5 mm and 6 mm, respectively
12	21667	M 54	Stomach	1 by 0.5 cm
13	11057	M 63	Stomach (2)	Largest—5 mm
14	11990	F 70	Stomach	1.5 cm
15	12253	F 61	Stomach	5 mm
16	12386	F 65	Stomach	4 by 2 by 1 cm
17	12493	F 78	Stomach	5 mm
18	12523	M 44	Stomach	2 mm
19	12731	M 65	Stomach	4 mm
20	12945	M 49	Stomach	6 by 4 by 4 mm
21	8289	M 56	Ileum	5 mm
22	10703	M 70	Ileum	1 cm
23**	12321	M 70	Duodenum and peripancreatic	Duodenal—5 cm Peripancreatic 0.5—1 cm

\*Found in a total of 5,869 autopsies. Incidence—0.39 per cent.

\*\*A most unique case. It is remarkable that a leiomyoma of considerable size in the duodenum, such as this, remained entirely silent during life.

masses, usually sessile, but often pedunculated, varying in size from less than 5 millimeters up to 20 to 30 centimeters in diameter and weighing as much as 6500 grams. Multiple growths are quite infrequent. They are

TABLE IV.—RESULTS IN 30 CLINICAL SMOOTH MUSCLE TUMORS

Site	Cases	Living with no disease	Died of disease	Operative death	Died of intercurrent disease	Living with disease
Stomach	8	4	3	1	0	0
Duodenum	2	0	2	0	0	0
Jejunum	1	1	0	0	0	0
Ileum	3	1	1	1	0	0
Meckel's diverticulum	1	1	0	0	0	0
Colon (left)	2	2	0	0	0	0
Rectum*	5	2	0	1	1	0
Retropertitoneal	8	1	3	2	0	2
Total	30	12	9	5	1	2

\*No follow up available in one case.

sharply circumscribed, but microscopically a definite capsule is seldom seen. The cut surface presents a grayish-pink, whorled or "watered-silk" appearance (Figs. 4 and 21). But, attributable chiefly to the relative avascularity of the tumor, regressive and inflammatory changes, such as fibrosis, necrosis, cavitation, hemorrhage, abscess formation, calcification, and cyst formation commonly supervene, so that the gross picture is usually quite variable (Figs. 2, 11, and 19).

Starting in the muscle coats, growth occurs toward or away from the lumen of the bowel, or in both directions, and Virchow, in 1863, first described leiomyomas as *inneren* (submucosal) or *ausseren* (subserosal). The preferred designation names the region involved, modified by the prefix endo- or exo-, as the case may be (e.g., *enteric leiomyoma of ileum*). In addition, the term "hour-glass" indicates the less common combined form and "intramural" describes the type which remains small, benign, and is always an incidental finding at operation or autopsy. These *intramural leiomyomas* are usually less than 1 centimeter in diameter and, although circumscribed, are practically never encapsulated.

With the exception of the tumors of the rectum, the overlying mucosa covering the submucosal masses commonly becomes ulcerated. Hemorrhage within the tumor frequently oc-

curs and, when associated with ulceration, the blood is discharged into the gastrointestinal tract (Figs. 4 and 8). Uncommonly, a neoplasm becomes necrotic or infected and perforates into the peritoneal cavity, with a resultant generalized peritonitis (Cases 2, 10).

The retroperitoneal tumors usually grow to the largest dimensions, are commonly less well defined and undergo similar degenerative changes. They almost always involve surrounding vital structures by direct extension and may even erode portions of the vertebral column (Case 29).

The histology of these tumors is much like that of smooth muscle tumors in other parts of the body with a few interesting variations. The smooth muscle cells with their myofibrils and an accompanying framework of connective tissue are arranged in bundles which tend to interlace (Figs. 6, 12, 15, 23). The spindle-shaped cells resemble smooth muscle cells to a greater or less degree, depending apparently upon rapidity of growth and regularity of mitotic division, but also upon phenomena of degeneration, so that the formation of bizarre or monster cells may be an indication either of atypical growth or degeneration (Figs. 3 and 20). A rather striking feature is the tendency of the nuclei to be aligned in palisade formation (Figs. 6, 9, 12, 15). It was observed in all but 6 of the tumors in our series. Seemingly it is much more common in this group of leiomyomas than in those found in other parts of the body. This fact, together with the tendency for the gastrointestinal leiomyomas to undergo patchy necrosis simulating the type B tissue of the neurilemmoma (Fig. 24), has led a number of writers (Gosset, et al., 1924; Abadie and Argaud, 1928; Jeanneney, 1933; Tierney, 1934; Ransom and Kay, 1940) to confuse smooth muscle tumors with nerve sheath tumors. One of the present writers was similarly misled and reported 3 gastric tumors as neurilemmomas (Stout, 1935; Cases 6, 17, and 30). These are now reclassified and included in the present group as Cases 35, 31, and 6, respectively.

This group of smooth muscle tumors differs from those in the uterus and subcutaneous tissues by the fact that they are not encapsulated, but their cells and fibers interdigitate

with uninvolved tissue at the periphery (Figs. 6 and 12). This makes it appear as if they were infiltrating growths, and no doubt has influenced some writers to classify them as malignant tumors. This is an unjustifiable criterion, for it occurs in practically all of the small intramural tumors found by chance at autopsy or operation (Fig. 25). This lack of encapsulation is of aid in differentiating the leiomyoma from the neurilemmoma, for the latter is always an encapsulated tumor.

One might suppose that the presence or relative absence of myofibrils could be used as a standard of relative differentiation, whereby it would be possible to judge degrees of malignancy. Unfortunately, this is not a reliable criterion. There are some tumors in this series, such as in Case 4, in which myofibrils could be found not at all, or only with the greatest difficulty and yet which have given no biological evidences of malignancy. On the other hand, Case 24 was always well supplied with myofibrils and yet is certainly malignant, since it metastasized. The demonstration of myofibrils is convincing proof of the nature of these tumors. We would emphasize the facts that good fixation and differential staining are essential to the accomplishment of this. Without them histological diagnosis is a matter of guesswork.

As in the uterine leiomyomas the size and shape of the cells is not necessarily a criterion of relative malignancy. A malignant leiomyoma may be composed of cells which show few differences from normal smooth muscle cells (Case 4, Fig. 6; Case 5, Fig. 9; Case 19, Fig. 23), while on the other hand some tumors in which bizarre cells are formed may not be clinically malignant (Case 15, Fig. 20). It is quite possible that in such cases the formation of bizarre cells is an indication of degeneration rather than hyperactivity.

The relative number of mitoses is an infallible indication of growth activity and relatively important as a criterion of malignancy. If two or more mitoses per high power field are present, one can feel fairly secure in predicting malignancy. But the converse of this is not true, for some clinically malignant tumors have shown relatively few mitoses (Cases 18 and 24).

The literature indicates that the benign tumor is eight times as frequent as the malignant in the stomach, while in the rest of the intestinal tract the ratio approaches 4 to 1. In the present series the ratio, when all cases are considered, is approximately 2 to 1, but if the 30 chance findings are excluded, the malignant leiomyoma occurred twice as often as the benign. Cases in which a histologically benign leiomyoma is associated with metastases have been reported (Hunt, 1923; Demel, 1926; Melnick, 1932), and in general the incidence of metastases is approximately 30 per cent of the malignant cases (Table I). Metastasis occurs most commonly to the liver, while rarely the lung and peritoneum are involved. Cellina (1931); Brink and Laing (1933); Pack and McNeer (1935); and Gottlieb and Reitman (1939) have reported metastases to the regional lymph nodes. We cannot comment upon this finding, since we have not personally studied these cases. Metastasis of malignant smooth muscle tumors primary in any part of the body to lymph nodes has never been observed by us. Generalized metastases involving distant organs have been reported in only two instances (Pack and McNeer, 1935; Ghon and Hintz, 1909).

Curiously, there are no reports of metastasis from a retroperitoneal smooth muscle tumor, but in the present series 3 of the 8 primary cases were associated with this complication. There is only 1 instance of metastasis from a rectal leiomyoma (Wright and Hall, 1932), but the incidence of recurrence in both regions is at least 25 per cent. The most plausible explanation for this seems to be that in these two regions a complete peritoneal barrier is lacking and even with apparently wide local excision of the tumor one or more occult nodules may be left behind.

#### SYMPTOMATOLOGY

The symptomatology by which these tumors manifest themselves is quite varied in severity and duration, and no typical or pathognomonic signs are available. In the interests of clarity, the clinical considerations are presented according to the regions involved.

*Stomach.* Although the endogastric and exogastric leiomyomas are of approximately

equal incidence, the degeneration and ulceration which almost always complicate the endogastric tumors account for the high frequency of hemorrhage. This occurs in over 50 per cent of the cases and is manifested by hematemesis, melena, and secondary anemia. Occasionally there may be bleeding in a case with an apparently intact mucosa and in some instances massive hemorrhage occurs in an exogastric tumor, being discharged into the gastric lumen through one or more sinus tracts. Often this is the only indicative sign and the attacks of hematemesis or melena may seem innocuous, being separated by weeks or even years of uneventful good health. However, the attacks ultimately increase in magnitude and frequency and the seriousness of the condition becomes apparent. Rarely, there is sudden onset of continuous hemorrhage which terminates fatally in a few days. This is the result of erosion of a large gastric vessel and such a catastrophe is strikingly represented in this series by Case 8 (Fig. 16).

Pseudo-ulcer symptoms consisting chiefly of epigastric pain and burning, nausea, vomiting, and anorexia, usually unrelated to meals, occur in 30 per cent and evidence of pyloric obstruction is of equal frequency. Willenbacher (1928) reported a case in which an apple-sized pyloric leiomyoma caused obstruction by intermittent ball-valve action and Barnett (1925) cited an instance of gastroduodenal intussusception as a result of a pedunculated leiomyoma arising in the cardia.

A palpable abdominal mass appears in 20 per cent and may be the only clinical finding, as in Case 7 (Fig. 14), while in 10 per cent there are vague complaints of weakness, fatigue, malaise, headache, and dizziness without special reference to the gastrointestinal tract. In the presence of coexistent disease in the stomach or elsewhere, the smooth muscle tumor may, and usually does, remain entirely silent.

Except in the rare highly malignant leiomyomas which run a fulminating course (Case 1, Figs. 2 and 3), cachexia, prostration, and marked weight loss are inconsequential factors and the latter seldom exceeds 10 to 15 pounds.

The exceptional case in which an exogastric tumor perforates into the peritoneal cavity

(Wells, 1924; Baumgartner, 1939; Case 2), is evidenced by pain and fever of variable duration, culminating in the sudden onset of signs of an acute abdomen.

There are no characteristic laboratory data associated with the neoplasm in any region.

Roentgenologic examination is a decided aid to diagnosis when properly applied and evaluated, but the typical configuration is common to all benign tumors and the correct diagnosis, when made, is based essentially on probabilities, since the leiomyoma is by far the most common of the benign tumors of the stomach. The following principal features, emphasized by Moore (1927) are worthy of mention:

(a) In the endogastric tumors we find: (1)

A central or marginal filling defect, usually rounded and smooth, occasionally exhibiting a crater shadow in the dome. Manual manipulation, in order to approximate the gastric walls, is essential, especially for small tumors. Sometimes a pedicle, if present, may thus be outlined. (2) There is no contraction or spasm of the stomach. (3) Peristalsis is usually interrupted and the gastric wall remains intact. (4) Rugae are not obliterated as in cancer, or thrown into convergent folds, as in ulcer. (5) Multiple growths are strongly indicative of benignity.

(b) In the exogastric tumors we find the following: Exogastric tumors manifest themselves by pressure or traction, thus producing a deformity which is likely to be misinterpreted as an ulcer or cancer. Negative roentgenograms do not exclude the possibility of a tumor.

It is noteworthy that in the series presented, a correct diagnosis of hour-glass gastric leiomyoma was made in one instance by Dr. Robert P. Ball (Case 7, Fig. 13), while Dr. Ross Golden correctly identified a case of endogastric malignant leiomyoma (Case 5, Fig. 7).

**Duodenum.** Tumors arising in this region are associated most frequently with symptoms simulating duodenal ulcer, and hemorrhage is the most significant sign. The exoduodenal are three times as common as the endoduodenal leiomyomas and evidence of obstruction is exceptional, in sharp contrast to the rather

high incidence of this complication in the rest of the small intestine.

The pars descendens is the site of origin in at least 50 per cent, but jaundice, as a result of obstruction of the common duct or ampulla of Vater, has apparently never been reported. In some cases, the tumor is responsible for constipation or diarrhea, or both, by compressing the overlying ascending or transverse colon and often it partially occludes the inferior vena cava or superior mesenteric artery, and death due to thrombosis or pulmonary embolism is of a remarkably high incidence (Case 9, also reported by Andersen and Doob in 1933; Brdiczka, 1931; Foshee and McBride, 1939; von Salis, 1920; Seymour and Gould, 1936).

A palpable tumor is present in 25 per cent of the cases and perforation of a degenerated leiomyoma into the peritoneal cavity (Case 10) is somewhat more frequent than with the gastric cases.

Roentgenologically, these tumors often manifest themselves as a deformity of the bulb or a filling defect, in common with other tumors in this region, and R. Golden (1928) suggested that these could be differentiated from gastric tumors by absence of a 6 hour residue.

**Jejunum and ileum.** In this region, hemorrhage, which usually cannot be localized, is again the most frequent finding. It may be slight or result fatally (Smith, 1937), but seldom is the small intestine suspected as the site of origin until a mass appears or there are symptoms of obstruction. The latter usually occurs late, but is precipitate and, although the exoenteric tumor is four times as common as the endoenteric, either type may be responsible for the intussusception, torsion, or angulation which produces the obstruction. Intussusception, in particular, is found in 30 per cent of the cases, accompanied by the usual signs.

Partial, slowly developing, increasingly severe obstruction accompanied by constipation, diarrhea, twinge-like local or generalized abdominal pain or cramps, tenderness, and occasional nausea and vomiting, is most often the result of gradual encroachment on the lumen by an endoenteric tumor. This type seldom attains the size of the exoenteric, but a palpable, freely movable mass is found in approximately one-half of all cases.

Degeneration of the tumor occurs here as often as elsewhere and is occasionally also responsible for generalized peritonitis as a result of perforation into the abdominal cavity (Feyrter, 1928; Kiefer, 1933; Goldberg, 1939; Lewis, 1939).

A Meckel's diverticulum has been the site of origin of a smooth muscle tumor in 8 reported instances and the associated symptoms are undifferentiated from those caused by the tumor elsewhere in the small intestine. Hoepfner (1912) reported a leiomyoma of a Meckel's diverticulum causing intussusception in a 9 year old boy and attempted to explain the mechanism involved. In the present series a ninth case (Case 15, Figs. 19 and 20) is added to those previously reported.

In the appendix, the symptoms most often resemble those due to acute appendicitis. The tip is the site of origin in 50 per cent and the largest tumor was 9.6 centimeters in diameter (Rosi, 1897). Only 15 cases have been reported; 14 tabulated by Koontz (1929), and the last described by Charache (1934).

Röntgenological studies are of limited value so far as these small intestinal tumors are concerned. They reveal intestinal obstruction, if present, but in no case has the tumor itself been outlined.

*Colon.* It has been indicated in the past by many observers that, in general, tumors of the left-sided colon usually produce obstruction, while on the right side, especially in the cecum, obstruction is rare. Smooth muscle tumors of the colon follow this rule and, since approximately 50 per cent are found in the cecum, obstructive signs are exceptional. Some of these are symptomless, while others present only a palpable mass, but in 2 cases (Jones, 1935; Trygstad, 1932), intussusception with complete obstruction occurred as a result of a cecal tumor. The less frequent left-sided leiomyomas are usually associated with signs of partial obstruction, whether the neoplasm is exocolonic or endocolonic (Case 17, Fig. 21).

The overlying mucosa is apparently less often ulcerated in this region than in the previously mentioned sites and degeneration and bleeding occur less frequently. A palpable freely movable mass appears in 40 per cent,

and a barium enema ordinarily will reveal a partial obstruction, if present.

*Rectum.* Almost all of the smooth muscle tumors of the rectum are endorectal, within easy reach of an examining finger, although extension anteriorly or posteriorly occasionally occurs. They are seldom larger than 5 to 6 centimeters in diameter, and the rectal mucosa is usually intact. Accordingly, bleeding is rare, while partial obstruction with a narrowed stool, constipation, tenesmus, difficult and painful defecation, diarrhea of glairy mucoid material, fullness, and sensation of a mass, in varying combinations, are habitually found. There may be marked rectal spasm and pain, often radiating to the thighs or back and when the tumor grows anteriorly, symptoms of urinary obstruction are prominent. In some instances, the tumor is pedunculated and may prolapse during defecation (Case 21). Heurtaux (1856) and Hunt (1921) recorded a number of these and Longuet (1898) described 2 cases in which the pedunculated tumor was expelled spontaneously with no apparent complications.

*Retropertoneum.* It is entirely impossible to decide before operation that a particular retropertoneal tumor is of smooth muscle origin. In common with all other tumors in this region, it usually attains marked bulk, often dissects the overlying mesenteries, and the associated symptomatology is always attributable to the mechanical effects of the mass. Pressure on nerves or plexuses results in various paresthesias or backache, radiating customarily to the thighs and legs. Edema of the lower extremities and occasional ascites are associated with venous embarrassment, while pressure on the intestinal tract may cause partial or complete obstruction, and involvement of the urinary system is responsible for frequency and urgency or obstruction with infection. Although it is probably more common than indicated, in only 1 other instance besides Case 29 was erosion of the lumbosacral vertebrae reported (Magoun, 1919).

By their very nature, it is clear that, except for the rare small omental leiomyomas, all these tumors are eventually palpable as indurated, fixed masses. It is necessary, however, carefully to exclude the possibility of

tumors or cysts of the spleen, kidneys, pancreas, rectum, or pelvic organs.

#### TREATMENT

Morgagni, in 1762, was apparently the first observer to describe a probable smooth muscle tumor; a gastric case, but it was not until 1890 that an attempt was made to remove such a mass surgically. The operation, by Kuntze, ended fatally; but 5 years later von Erlach successfully resected a 5400 gram gastric leiomyoma in a 36 year old female. To the present time this has remained the only available form of therapy, since neither roentgen therapy nor radium implantation have any appreciable effect upon the tumor.

Gastric and intestinal leiomyomas (with the exception of those originating in the duodenum) are most amenable to excision or resection, and the operative mortality varies directly with the experience of the surgeon and the presence or absence of complications. The choice of procedure is limited to local excision through gastrotomy or partial resection followed by anastomosis, but in rare instances the tumor will prove technically inoperable. The presence of metastases, unless widespread, is no contraindication to surgery, but in such a case the primary tumor must be resected as widely as possible. In most cases no metastases are present and an attempt at deciding the question of malignancy should be made by frozen section. Admittedly, this is very difficult, but if malignant characteristics can be readily demonstrated or if reasonable doubt as to benignancy exists, a partial resection should be accomplished. If the tumor appears benign, and local excision is decided upon, a generous ring of stomach or bowel wall beyond the apparent limits of the tumor should be excised with it, since these tumors are almost never truly encapsulated. Exception must be taken to the recent inference by Lahey and Colcock (1940) that, generally, radical subtotal gastrectomy is indicated in gastric cases. If the tumor is carefully and properly evaluated, conservative removal will be adequate and least disturbing to the patient's physiological economy in the majority of instances.

Where the duodenum is the site of origin, the usual involvement of adjacent vital struc-

tures seriously complicates the surgical problem, and in some instances the surgeon may be loath to attempt removal. However, if at all feasible, a partial resection, modified as necessitated by individual characteristics, remains the patient's only hope. Fortunately, most of these tumors arise in the readily accessible pars descendens.

Rectal leiomyomas have been treated in the past most often by enucleation or, if pedunculated, by excision through the pedicle. Hunt (1921) summarized a number of previous cases, in which it appeared that enucleation or simple excision was entirely adequate, but more recently, critical observers such as Rankin and Larson (1932) and Barga and Dixon (1934) have found that recurrence followed excision in an uncomfortably large percentage and, because of this, increasingly radical removal was necessary.

With the exception of the pedunculated tumors, the possibility of recurrence is not governed by the benignancy or malignancy of the histological picture, and it has been pointed out that occult nodules may remain even after extensive excision. Therefore, in view of the fact that it is impossible to decide definitely in advance whether or not the tumor will reappear, it is clear that radical surgery is indicated and all leiomyomas of the rectum, except for the occasional pedicled case, must be treated by abdominoperineal resection or its modification, permanent colostomy, followed by perineal proctectomy. If recurrence does eventuate, it is most likely to appear in the operative site (Case 18), and may be readily dealt with by simple excision without subjecting the patient to repeated serious surgery.

The exceptional pedunculated leiomyoma can be excised locally through its pedicle, since the possibility of recurrence in such a case appears to be remote.

Retroperitoneal tumors in general are frequently inoperable and, as Phillips (1934) has indicated, the immediate mortality in those cases in which removal is attempted is beyond 40 per cent. Often segments of small and large intestines must be removed with the mass, because of interference with blood supply and, if a particular tumor can be excised, the most radical excision possible is indicated. If com-





Fig 1. Case 1. Roentgenogram of malignant leiomyoma of stomach. The tumor has caused an irregular filling defect along the greater curvature near the cardiac end. Barium has filled the excavation shown in Figure 2.



Fig 2. Case 1. Malignant leiomyoma of stomach (12 by 10 by 6 cm). The tumor lies in the posterior wall near the greater curvature with the pylorus at the left. There is a deep excavated ulcer which penetrates through the mucosa into the tumor.

plete extirpation cannot be achieved, it is advantageous and advisable to remove as much of the tumor as possible by morcellation. Although this is only temporarily effective, it will usually make the patient more comfortable for an indeterminate period than if the entire tumor is left *in situ*. Case 30 in the present series is the only instance on record in which a retroperitoneal smooth muscle tumor, untreated, did not continue to grow and terminate fatally. Amazingly enough, in this particular case, the tumor is actually smaller at present (7½ years following biopsy) and entirely symptomless.

#### PROGNOSIS

The literature does not present a conclusive foundation on which prognosis may be based, since in only a few instances is an adequate follow-up available and often the diagnosis of malignancy is not clearly established. In general, however, it may be stated that proper surgical treatment of the benign smooth muscle tumor will result in a cure, unless the tumor is rectal or retroperitoneal. In the latter instances, and occasionally with a duodenal leiomyoma, the probability of total cure is

rather remote, for reasons here indicated, and the prognosis must be extremely guarded.

The malignant leiomyoma is usually of low grade malignancy and if adequately treated, even in the presence of metastases, the patient may enjoy many years of uneventful health. Demel (1926) told of a 42 year old female patient in whom he found a 12 by 11 centimeter metastatic hepatic nodule of smooth muscle tissue. There was apparently no primary site and the metastatic nodule was excised. It was not until 2 years later, at autopsy, that the original tumor in the jejunum was seen, and there were many additional large liver metastases.

However, where the histological picture indicates a poorly differentiated tumor, with many mitoses and bizarre forms, the duration of life, even with radical removal, appears to be little more than a year or two following the onset of symptoms. Fortunately such cases are uncommon. With this exception, it appears that the benign and malignant types are often similar in action and therefore no sharp clinical distinction has been made between the two.

In the present series, several of the cases have approached a 10 year follow-up, and Judd and Hoerner (1936) reported a stomach case alive 22 years after operation, but more cases must be followed for longer periods before definite conclusions can be drawn. It can be stated, however, that most of these tumors

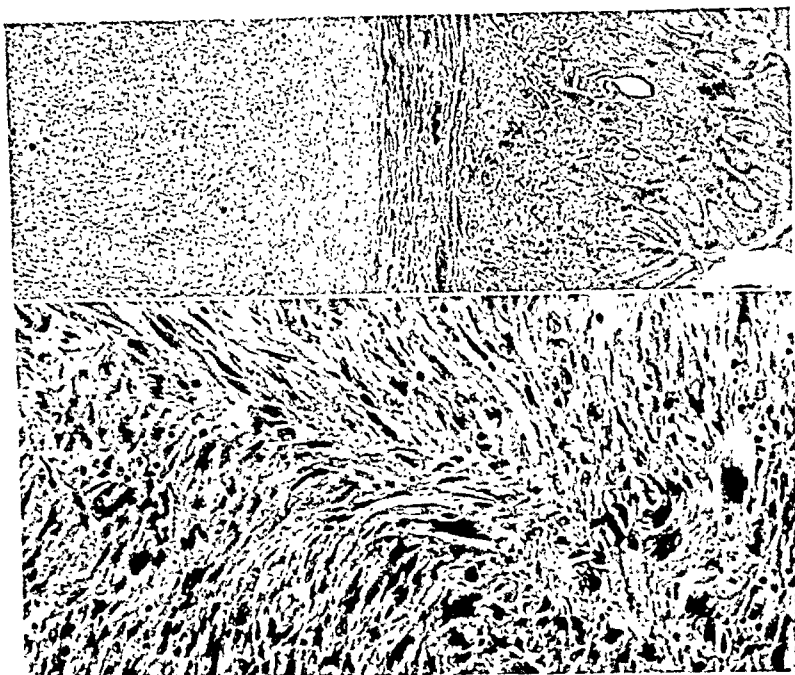


Fig. 3. Case 1. Malignant leiomyoma of stomach. Above, Relationship of tumor to the submucosa and mucosa. Below, The tumor is composed of interlaced bundles of spindle cells showing mitoses and monster forms.

appear to be less malignant than the majority of cancers, and if recognized early enough and treated properly they usually offer at least a fair prognosis.

#### CASE REPORTS<sup>1</sup>

##### *Stomach*

CASE 1. S. P. 35506. Unit Hist. No. 67090. P. L., a 43 year old white Italian male was first admitted to the Presbyterian Hospital, October 26, 1926, with a 5 months' history of indigestion, feeling of heaviness, constipation, headache, marked nausea, and lower abdominal cramps, relieved by soda. Jaundice at onset, then chills and afternoon fever intermittently. Vomiting on two occasions: once foul, coffee-ground material. No melena. There was marked weakness, dyspnea and a loss of 20 pounds in weight. Symptoms were aggravated during previous 3 weeks.

Examination revealed a poorly nourished male showing evidence of marked weight loss, dyspnea and pallor. Skin icteric. Epigastric tenderness was well defined, but no masses were palpable. Stool guaiac, + + + +. Barium series showed a broad, irregular filling defect in the greater curvature of the stomach about 2.5 centimeters below the upper surface of the fundus (Fig. 1). Peristalsis did not pass

over the greater curvature. A diagnosis of carcinoma of the stomach was made and surgery was advised, but, with symptomatic improvement, the patient rejected this advice and left the hospital November 13, 1926.

He returned at the end of 3 months quite improved, and on February 14, 1927, a sleeve resection of the gastric tumor was performed by Dr. Fordyce B. St. John. The tumor was firm, lobulated, and chiefly endogastric, lying in the posterior wall of the pars media near the greater curvature. There were several large subserosal projections, and the overlying vessels were quite prominent and markedly distended. The mass measured 12 by 10 by 6 centimeters and there was a crater-like excavation in its mid-portion measuring 5 by 4 by 2 centimeters. There was no evidence of metastasis (Fig. 2).

Microscopically, the tumor was sharply circumscribed, lying between the submucosa and muscularis. It was composed of freely interlaced bundles of large, elongated cells, with hyperchromatic nuclei. Mitoses averaged 1 in every 2 high power fields and there were scattered bizarre forms as well as occasional multinucleated cells (Fig. 3). Preparations adequate for the demonstration of myofibrils were not available.

Diagnosis: Malignant leiomyoma of stomach.

The immediate postoperative course was satisfactory, and the patient was discharged March 24, 1927,

<sup>1</sup>The illustrative cases are presented in detail.

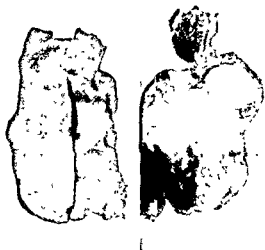


Fig. 4. Case 4. Malignant leiomyoma of stomach (6.5 by 4.5 by 4 cm.). The tumor is covered by thin mucosa. In the line of incision are 3 small ulcerations. The cut surface presents a glistening "watered silk" appearance with one large area of hemorrhage. This communicated with the gastric lumen through one of the ulcerations.

greatly improved. He gained 17 pounds during the first month, but soon began to lose ground rapidly and was again admitted November 19, 1927, complaining of loss of strength, dyspnea, pain in incisional line, and loss of 10 pounds in weight. A 2 centimeter nodule was found in the midportion of the incisional scar and a roentgenogram revealed marked pulmonary metastases. He was given symptomatic care, his condition was evidently hopeless, and he was discharged November 27, 1927. He went rapidly downhill, developing a severe cough with orthopnea, and expired at home January 4, 1928, 20 months after onset of symptoms and 11 months following resection of the tumor. No autopsy could be obtained.

Final diagnosis: Malignant leiomyoma of stomach with metastases to lungs and probable implantation in abdominal scar.

CASE 2. S. P. 56225. Unit Hist No. 433406. B. H., a 57 year old white American male was admitted to the Presbyterian Hospital, October 20, 1934, with a 2 months' history of a right upper quadrant abdominal mass, weakness, anemia, constipation, and elevated temperature. Seven months before admission, there had been a sudden onset of severe right lower quadrant abdominal pain, and a large tender mass in this area. He was operated on in Newark, New Jersey, and an appendiceal abscess containing the remnants of a perforated appendix was found. The upper abdominal mass developed soon after recovery.

Examination revealed marked anemia, a well defined upper abdominal mass, and an enlarged, nodular liver. A barium series showed no definite disease within the gastrointestinal tract.

On December 15, 1934, an exploratory laparotomy was performed by Dr. Allen O. Whipple. The mass itself could not be resected, and there were two metastatic nodules in the liver. The tumor was biopsied. Roentgenotherapy was instituted after operation, but proved of no value. The patient went downhill rapidly, developed terminal signs of a diffuse peritonitis, and expired on January 20, 1935, 5 months after onset of symptoms.

At autopsy (No. 11724), the tumor was found in the lower half of the stomach. It was a degenerated, friable, exogastric mass measuring 20 by 12 centimeters. An ulceration in the overlying mucosa led directly into a central abscess cavity which had further ruptured into the peritoneal cavity, resulting in a generalized peritonitis. Two large, firm, whitish metastatic nodules were in the right lobe of the enlarged liver.

Microscopically, the biopsy consisted of tumor tissue invading the gastric muscularis and projecting slightly into the lumen of the stomach as an ulcerated mass. It was made up of parallel, interlaced bands of smooth muscle cells varying considerably in size and shape. The nuclei were often hyperchromatic and a number of multinucleated forms were seen. Myofibrils could not be clearly demonstrated. Mitotic figures averaged 1 in every high power field and occasionally assumed bizarre forms. There was a considerable fibrous stroma containing a moderate number of small blood vessels. Autopsy sections were similar.

Diagnosis: Malignant leiomyoma of stomach with metastases to liver.

CASE 3. S. P. 72684. 72954. Unit Hist No. 565708. Autopsy No. 13,237. J. B., a 43 year old obese colored male was admitted to the medical service of the Presbyterian Hospital from the Vanderbilt Clinic, November 19, 1930, for a thorough gastrointestinal work-up. He had complained for a year of gas pains, unrelated to meals, and flatulence. He had been treated in the clinic for mild secondary anemia. In the last 3 months he had developed a tender mass in the left upper quadrant and had lost a total of 35 pounds during the year.

Physical examination revealed a firm, movable, somewhat tender, nodular abdominal mass on the left side, extending from under the costal margin to the iliac crest. Temperature, pulse, and erythrocyte sedimentation rate were moderately elevated and there was a secondary anemia. Stool guaiac, + + + +.

Five days after admission, a roentgenogram revealed a large mass behind the stomach displacing it forward and causing a pressure defect along the greater curvature posteriorly. It appeared to represent an intra abdominal tumor secondarily invading the stomach and on November 29, 1930, a biopsy specimen was removed from it.

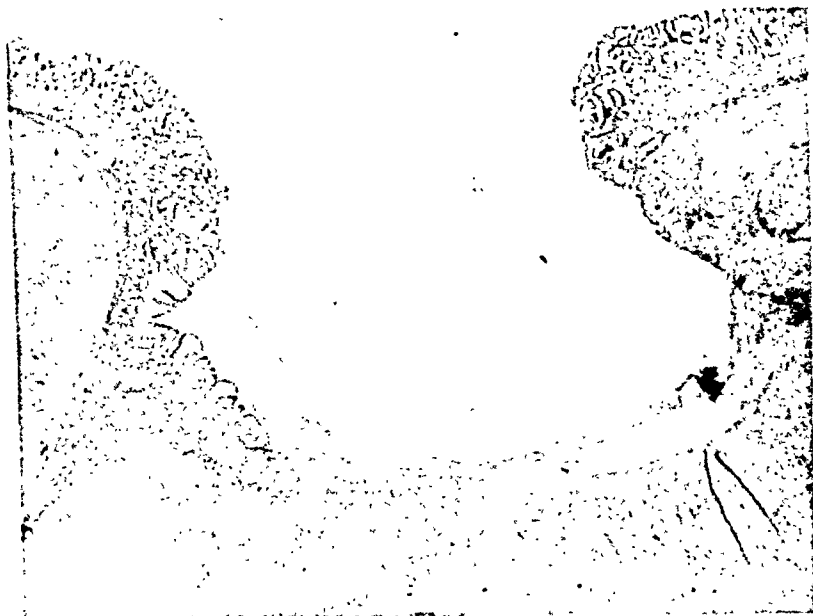


Fig. 5. Case 4. Malignant leiomyoma of stomach. One of the ulcerations in the tumor.

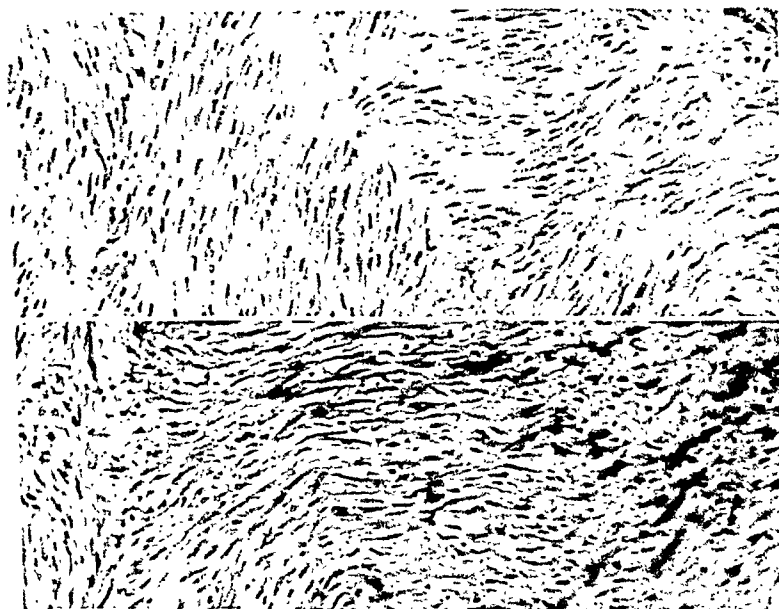


Fig. 6. Case 4. Malignant leiomyoma of stomach. The tumor is composed of interlaced bundles of spindle cells. Palisaded nuclei are shown in the area above and interdigitation of tumor with the muscle coat below.



Fig 7 Case 5 Roentgenogram (recumbent, oblique view) of malignant leiomyoma of stomach (diagnosis made before operation). The tumor makes a smooth, rounded filling defect, and barium fills an ulcer crater in the dome.

The biopsy was composed of elongated, inter-twined and whorled smooth muscle cells, with plump nuclei occasionally arranged in atypical palisades. There was some irregularity in cellular size and shape, but mitoses were scarce. Myofibrils could not be demonstrated. The connective tissue stroma was scanty, poorly vascularized, and there were scattered areas of necrosis.

Diagnosis: Malignant leiomyoma of stomach.

Following the biopsy examination, the advisability of further surgery was the subject of much discussion, but it appeared that intragastric hemorrhage was becoming more severe, the patient's condition was increasingly critical, and the prognosis apparently hopeless. It was therefore decided that a desperate chance had to be taken and on December 29, 1939, Dr Hugh Auchincloss attempted to remove the tumor. It measured 20 by 13 by 7.5 centimeters and weighed 985 grams. It was almost entirely necrotic and arose in the posterior aspect of the stomach along the greater curvature communicating with its lumen through a broad sinus tract. It grew exogastrically, involving the pancreas, transverse mesocolon and partially surrounded the aorta in this region. A block resection of the tumor and involved sections of stomach, pancreas, and transverse colon was carried out, but the small portion in the region of the aorta had to be left *in situ*. The viscera were repaired, and the patient left the operating room in fair condition.

For the first 3 days after operation he held his ground, but on the fourth day he became jaundiced, developed unmistakable signs of bronchopneumonia and, in spite of heroic measures, expired the following morning, January 3, 1940.

At autopsy, a localized left upper quadrant peritonitis, infarct and gangrene of spleen, residual tu-



Fig 8 Case 5 Malignant leiomyoma of stomach (6 by 5 by 4.5 cm). An area of ulceration in the overlying mucosa opens into a central cavity surrounded by tumor tissue showing small foci of degeneration.

mor, and bilateral lobular pneumonia were the principal findings.

CASE 4 S. P. 59599 Unit Hist No 473180 J. A., a 49 year old white American male was admitted to the medical service of the Presbyterian Hospital on December 8, 1935, with a 4 years' history of indigestion, irregularly after meals, relieved occasionally by food and soda. For the previous 3 months he had experienced attacks of fullness and burning in the epigastrium, starting one hour after meals and occasionally at night. There was increasing weakness and 2 days before admission he had several tarry stools. On day of admission he experienced an attack of fainting.

There was pain and hyperesthesia over the lower sternum, anemia, elevated erythrocyte sedimentation rate and stool guaiac, ++++. He improved somewhat after being placed on a Sippy diet, but a barium series showed a smooth mass projecting forward in the posterior wall of the fundus of the stomach with a small crater shadow in its center. The tumor was considered to be either benign or a sarcoma, and the patient was transferred to the surgical service for operative treatment.

Operation on January 10, 1936 by Dr Fordyce B. St. John, revealed a 6.5 by 4.5 by 4 centimeter endogastric, well circumscribed, firm, nodular tumor in the posterior wall of the fundus of the stomach. The overlying mucosa was ulcerated in 3 areas centrally, and the cut surface presented a glistening, "watered silk" appearance, with areas of degeneration, cavitation, and hemorrhage directly beneath and continuous with the ulcerations (Fig 4). No evidence of metastases was noted and a local resection of the mass was performed.

Microscopically, the tumor was composed of interlaced bundles and sheaves of oval or spindle shaped smooth muscle cells, containing elongated palisaded vesicular nuclei. The cells were in the main fairly uniform in size, shape, and staining characteristics, but in one nodular area a group of closely packed, oval cells presented marked irregularity, with here and there a multinucleated form. Mitoses averaged 1 in every 3 high power fields. Myofibrils were not

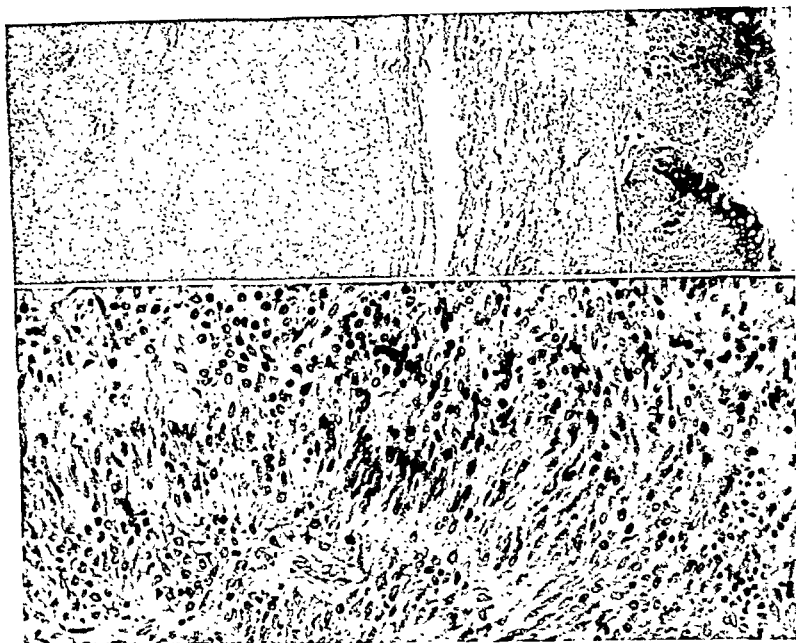


Fig. 9. Case 5. Malignant leiomyoma of stomach. The topography of the tumor is shown above. Below are the plump, closely packed smooth muscle cells with palisaded, vesicular nuclei and a scanty fibrous stroma.

demonstrated. In some places, at the margins, bundles of tumor cells interdigitated with strands of normal smooth muscle (Figs. 5 and 6).

Diagnosis: Malignant leiomyoma of stomach.

After operation the patient's course was very stormy. He developed a wound abscess, followed by subphrenic abscess and pyo-pneumothorax. These complications were treated surgically, but gastric and pleural fistulas remained. However, there was satisfactory slow improvement and he was discharged August 2, 1936, 207 days after operation. The fistulas gradually closed and, except for a ventral hernia, his general condition was quite satisfactory. At present, 5 years after operation, and 9 years after onset of symptoms, he is gaining weight and shows no evidence of recurrence.

CASE 5. S. P. 72308. Unit Hist. No. 228716. C. S., a 45 year old white Irish male was admitted to the Presbyterian Hospital on October 22, 1939, with a 3 year history of repeated bouts of melena and hematemesis with progressive anemia. He was treated symptomatically for a supposed duodenal ulcer.

Physically, except for slight epigastric tenderness, no positive findings were elicited. A barium series was done and a large, rounded, smooth tumor was seen in the fundus of the stomach, attached by a broad pedicle to the posterior wall and projecting into the lumen. A crater which measured 2 centimeters was noted in the margin opposite the pedicle (Fig. 7).

Diagnosis: Malignant leiomyoma of stomach (Dr. Ross Golden).

Operation by Dr. Fordyce B. St. John on October 25, 1939, revealed a rounded, rather firm, endogastric tumor measuring 6 by 5 by 4.5 centimeters, arising in the posterior wall near the cardia. It was entirely covered by intact mucosa except in the central portion, where there was a 1.5 centimeter circular opening, with rounded, piled-up edges, leading directly into a 2.8 by 2.5 by 2 centimeter cavity. The walls of the latter were shaggy, rough, and grayish white, while the surrounding tissue was firm, homogenous, and reddish-gray. The main portion of the tumor was composed of glistening, grayish-white tissue arranged in irregular strands (Fig. 8). There was no evidence of metastasis. The mass was excised locally, and the stomach was closed. Recovery was entirely uneventful and the patient was discharged on the seventeenth day after operation. One year following operation, and 4 years after onset of symptoms, he is in excellent condition, with no complaints and no evidence of recurrence.

Microscopic examination revealed a highly cellular, fairly homogenous tumor made up of large elongated or spindle cells, with oval, vesicular nuclei arranged in palisades, and set in a scanty fibrous stroma. There was some variation in cellular and nuclear size and staining, with occasional mitotic figures (Fig. 9). Well defined myofibrils were seen in many places. There was no evidence of capsule formation, but the edges were fairly distinct and the



Fig. 10. Case 6. Roentgenogram of hour glass leiomyoma of stomach. The endogastric portion makes an irregularly, rounded filling defect. Peristalsis was visualized fluoroscopically in the immediate vicinity.

tumor was entirely confined within the muscularis, except in the region of the ulceration.

Diagnosis. Malignant leiomyoma of stomach.

CASE 6 S. P. 51874 Unit Hist No. 384493. F. R., a 50 year old white Colombian female was admitted to the medical service of the Presbyterian Hospital, July 3, 1933, with a history of dyspnea and gas after meals, for many years. She also had had cramp like right upper quadrant pains, but none in the past 2 years after an attack of jaundice. For the past 2 months she had become anemic and suffered with increased weakness and occipital headaches. Swelling of face and ankles and occasional vomiting occurred during the previous 2 weeks.

Physical examination revealed a definite pallor, tongue smooth at edges, and a moderately enlarged heart. There was tenderness in the region of the gall bladder. Stool guaiac, ++++. Roentgenography and fluoroscopy revealed a pedunculated mass arising from the posterior wall of the stomach just behind the cardiac orifice. Peristalsis was visible in the immediate vicinity (Fig. 10).

Diagnosis. Benign polyp of stomach (Dr. Ross Golden).

The patient was transferred to the surgical service and at operation on July 20, 1933, Dr. Fordyce B. St. John found an hour-glass tumor in the anterior wall of the stomach, high in the fundus, which he treated by simple local excision and gastrotomy. There was no evidence of metastases. It was a firm, nodular mass, the endogastric portion measuring 4.5 by 3.5 by 2.5 centimeters, while the exogastric portion was 2.8 by 2 by 1.8 centimeters. The overlying mucosa was irregular and cryptic with several small sinuses extending into the mass and ending in an 8 by 4 millimeter cavity filled with a small amount of dried blood. Elsewhere the tumor tissue presented an indurated grayish white, occasionally whorled,

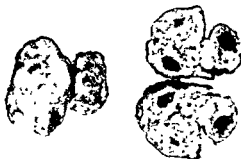


Fig. 11. Case 6. Leiomyoma of stomach (hour glass type). The larger portion (4.5 by 3.5 by 2.5 cm.) was endogastric. It is covered by flattened mucosa in which are crypt like ulcerations. The smaller exogastric mass (2.8 by 2 by 1.8 cm.) is nodular and covered by serosa. The cut surface at the right shows areas of hemorrhage and necrosis.

cut surface containing scattered hemorrhages (Fig. 11).

Microscopically, the tumor was composed of irregularly interlaced bundles of spraddle shaped smooth muscle cells arranged as nodular whorls. Occasionally the tumor penetrated the muscularis mucosae. The nuclei in most places were elongated, often arranged in palisaded fashion, and myofibrils were scattered throughout. No mitotic figures were seen. The dense fibrous supporting stroma was moderate in amount, containing relatively few blood vessels, and there were many areas of serous degeneration. In some places a very thin fibrous capsule defined the tumor (Fig. 12).

Diagnosis. Leiomyoma of stomach.

The patient made an uneventful recovery and, when last seen in December, 1938, 7½ years after operation, her condition was excellent. She was lost to follow up after that date.

CASE 7 S. P. 68707. Unit Hist No. 326213. J. B., a 44 year old British West Indian colored female was admitted to the Presbyterian Hospital on October 15, 1938, with a history of a slowly growing mass in the left upper quadrant during the past 4½ years. Recently there was a sensation of heaviness, but otherwise the tumor was entirely asymptomatic.

On examination, a freely movable, smooth, non-tender 11.5 by 7 centimeter mass was palpable in the left upper quadrant. Percussion elicited tympany anterior to the mass. Except for a lower midline scar of a previous appendectomy, there were no other remarkable findings. A barium series revealed a rounded tumor mass 6 centimeters in diameter projecting into the lumen from the anterior wall of the pars media (Fig. 13). Since the mass was also palpable anteriorly, it appeared that this was an hour glass tumor arising within the stomach and, with a history of 4½ years' duration, it was considered a benign growth.



Fig. 12. Case 6. Leiomyoma of stomach (hour-glass type). The tumor is composed of interlaced bundles of smooth muscle cells and a fibrous stroma. It has broken through the muscularis mucosae (left). At the right are shown magnified tumor cells with some tendency to palisade their elongated nuclei.

Diagnosis: Leiomyoma of stomach (Dr. Robert P. Ball).

At operation, on October 21, 1938, Dr. Allen O. Whipple found a firm, hour-glass tumor originating in the anterior wall of the pars media, near the lesser curvature. The smaller endogastric mass measured 6 by 5 by 3.5 centimeters and was covered by intact, normal-appearing mucosa. The larger exogastric portion measured 12 by 8 by 6 centimeters, and the overlying serosa contained many tortuous, engorged blood vessels. Several dense adhesions extended from it onto the stomach (Fig. 14). On section there were many areas of degeneration, while in other places the tissue presented a grayish-white, "watered-silk" cut surface. There was no evidence of metastases. A partial gastric resection followed by a posterior Pólya gastroenterostomy was performed.

Microscopic examination revealed a well circumscribed tumor composed of whorled, interlaced bundles of highly differentiated, elongated, smooth muscle cells with palisaded nuclei. Many myofibrils were present and mitotic figures were very rare (Fig. 15). There was a moderate amount of poorly vascularized connective tissue stroma, arranged mostly as fibrous trabeculae and several areas of necrosis were seen.

Diagnosis: Leiomyoma of stomach.

The patient's recovery was uneventful and at present, 2 years following resection and 6½ years after the appearance of the tumor, her condition is excellent.

CASE 8. Unit Hist. No. 72585. J. B., a 63 year old white American female was admitted to the

medical service of the Presbyterian Hospital on July 11, 1928, with a 10 day history of indigestion and cramp-like epigastric pains. During the previous 2 days there were several tarry stools, together with nausea and hematemesis, as well as an attack of unconsciousness lasting 45 minutes. She lost 5½ pounds in the past year.

Physical examination revealed no positive findings except for secondary anemia and an elevated pulse. There was slight improvement with clyses and a transfusion, but on the seventh day there was sudden onset of deep shock, and the patient expired.

At autopsy (No. 10035), the stomach was found filled with a large amount of tarry mucoid material and in the posterior wall, 1 centimeter from the lesser curvature and 8 centimeters distal to the cardia, there was a stony-hard, well circumscribed grayish-white, slightly exogastric mass measuring 2.3 by 2 centimeters. In the overlying mucosa there was an ulcer crater with raised edges, and clearly visible at the periphery were the openings of two blood vessels.

Microscopically, the tumor was composed of interlaced bundles of smooth muscle cells with elongated or oval, palisaded nuclei, and numerous myofibrils. No mitotic figures were seen. The fibrous stroma was scanty and vascularity was slight. It was partially surrounded by a very thin fibrous capsule and the center of the mass was occupied by a well defined area of degeneration with cavitation. At the edge of the shallow mucosal ulceration the open mouth of one of the eroded blood vessels was seen (Fig. 16).

Diagnosis: Leiomyoma of stomach (degeneration and erosion of gastric blood vessels).





Fig 13 Case 7. Roentgenogram of hour-glass leiomyoma of stomach (diagnosis made preoperatively). The endogastric component of the tumor makes a smooth, rounded filling defect near the cardia, while the exogastric portion is suggested by the distortion of the lesser curvature.

#### Duodenum

CASE 9. Unit Hist No 352745. Autopsy No 11053 (Previously reported by Andersen and Doob (1933). J O, a 37 year old white American male



Fig 15. Case 7. Leiomyoma of stomach (hour-glass type). The tumor is made up of interlaced bundles of smooth muscle cells with palisaded nuclei and well developed myofibrils shown magnified below.



Fig 14 Case 7. Leiomyoma of stomach (hour glass type). The posterior wall of the stomach has been removed showing the pylorus at the right and the bilobed tumor high on the lesser curvature. The smaller endogastric portion covered by smooth mucosa measures 6 by 5 by 3 centimeters. The larger exogastric part covered by serosa with dilated veins is 12 by 8 by 6 centimeters.

was admitted September 14, 1932, with a 5 weeks' history of tarry stool, weakness, pallor, loss of weight, shortness of breath and a right-sided abdominal mass. He also had swelling of the feet and ankles, especially the right, and a severe "squeezing" pain in the right leg for the past 8 days. He had been hospitalized 3 years previously for similar, although less severe, complaints and at that time a diagnosis of duodenal ulcer was made. There was no evidence of this by roentgenogram, but he improved on a Sippy diet and liver therapy. In the intervening years he had repeated gastric hemorrhages, but recovered from each.

Physical examination revealed an acutely ill, anemic young male, with elevated temperature. A slightly tender mass in the right upper abdomen extended 3 to 4 centimeters below the liver edge. It was indurated, irregular, well circumscribed, and apparently attached to the retroperitoneal tissue. A barium series showed this mass to be apparently outside the gastrointestinal tract. On September 18, he had a fainting attack and on the 20th, while on a bed pan, he felt weak, dizzy, and gasped for air. He passed a large tarry stool, went into extreme shock, and died shortly thereafter.

At autopsy, the mass occupied the center of the abdominal cavity, compressing the overlying bowel. It extended slightly more to the right and was adherent to the capsule of the lower pole of the right kidney. It was adherent to, and pulled the duodenum down to the level of, the lower lumbar vertebrae. It measured 18 by 15 by 12 centimeters, with

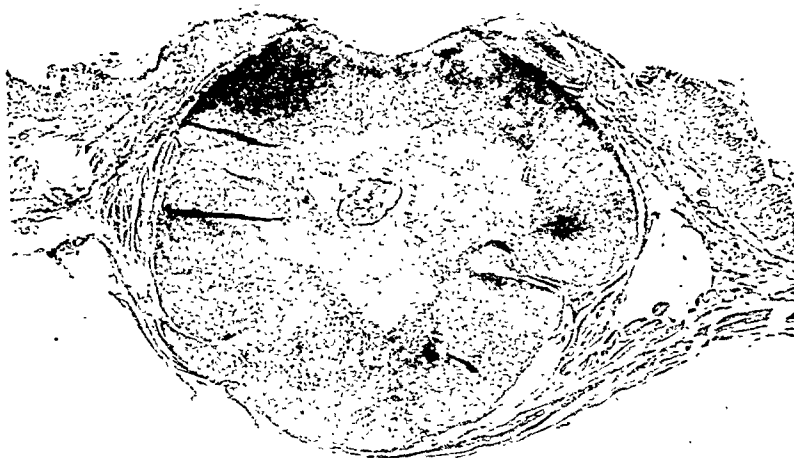


Fig. 16. Case 8. Leiomyoma of stomach. The 2 centimeter tumor expands the muscular coat, and ulceration through the mucosa has excavated it superficially. The ulceration also eroded two large submucosal blood vessels and caused fatal hemorrhage. One is shown adjoining the tumor.

central degeneration and cavitation communicating with the duodenum by a 3 centimeter opening at the level of the ampulla of Vater. It compressed the inferior vena cava and was in contact with the head of the pancreas, but did not invade it. Three nodules, the largest measuring 5 centimeters in diameter, were found in the liver, and the immediate cause of death was thrombosis of the common iliac veins with pulmonary embolism.

Microscopically, the tumor was composed of interlaced bundles of smooth muscle cells with elongated, palisaded nuclei showing variation in size, shape, and staining. Myofibrils were occasionally seen and mitoses were uncommon. There was a moderate amount of fibrous stroma containing few blood vessels. The mass was rather well circumscribed, and the overlying mucosa was everywhere intact, except in the region of the sinus tract. The nodules in the liver were made up of similar tissue.

Diagnosis: Malignant leiomyoma of duodenum, with metastases to liver. Thrombosis of common iliac veins. Embolism of pulmonary arteries.

CASE 10. Unit Hist. No. 539590. Autopsy No. 12666. C. S., a 53 year old white German male was admitted January 7, 1938, with a history of generalized abdominal pain for 9 hours and fecal vomiting for 7 hours. Onset of illness 3 months previously with exertional dyspnea, ankle edema, afternoon fever, and intermittent lower abdominal, cramping pain.

Examination revealed an acutely ill, markedly anemic patient with generalized abdominal tenderness and rebound tenderness; marked distention, tympany around diaphragm, and flatness in the

flanks; no fluid waves. Stool guaiac, + + + +. A flat plate showed intestinal ileus. He went rapidly downhill and died within 3 hours.

Clinical diagnosis: Mesenteric thrombosis. Bacterial endocarditis.



Fig. 17. Case 9. Malignant leiomyoma of jejunum (hour-glass type). The tumor interdigitates with the fibers of the muscularis from which it arose. The picture does not show the ulceration in the larger endoenteric portion. Three areas of calcification are shown.

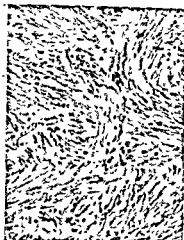


Fig 18 Case 14 Leiomyoma of ileum (6 by 6 by 5 cm) The gut and tumor have been bisected longitudinally. A mucosal ulceration leads into a 2.5 centimeter cavity. Most of the tumor is exoenteric. It is composed of interlaced bundles of relatively well differentiated smooth muscle cells and fibers.

At autopsy, a large, fluctuant retroperitoneal mass lay between the bifurcation of the aorta below and the postero-inferior border of the stomach above, reaching laterally to both renal pelves. The central portion was filled with foul, hemorrhagic, necrotic, friable material, and communicated with the lumen of the dilated descending portion of the duodenum via a 7 by 5 centimeter perforation in its postero-lateral aspect. The horizontal and ascending portion

of the duodenum, as well as the pancreas, appeared to be incorporated within the mass, and the pancreas itself could not be identified. Posteriorly, the mass lay anterior to the inferior vena cava and abdominal aorta, but neither was involved. There was an acute diffuse fibrinopurulent peritonitis with 500 cubic centimeters of serosanguineous fluid from which *Streptococcus viridans* and *Bacillus coli* were cultured, but no definite point of perforation of the mass could be identified. No evidence of regional or distant metastases was found. The heart showed evidences of aortic stenosis with insufficiency and enlargement.

Microscopically, the tumor was composed of well differentiated, uniform, elongated smooth muscle cells with palisaded nuclei and a moderate amount of fibrous stroma. Definite myofibrils were noted throughout, and no mitoses were seen. Vascularity was poorly developed, and there were many areas of degeneration and necrosis.

Diagnosis: Leiomyoma of the duodenum. Acute diffuse peritonitis. Pancreatic fat necrosis. Acute rheumatic endocarditis. Aortic stenosis and insufficiency.

#### *Jejunum and Ileum*

CASE 11 P & S No 12564 P S, a white American male, aged 60, was admitted to St. Luke's Hospital, Utica, New York, on July 2, 1932, with a 3 days' history of tarry diarrhoea and fainting spells associated with weakness. Previous general health had been very good. Average weight, 168 pounds and he had gained during last 2 years. There was no definite evidence suggestive of ulcer or acute abdominal catastrophe and, except for an evident anemia, the physical examination brought to light no positive findings.



Fig 19 Case 15 Malignant leiomyoma of Meckel's diverticulum. The degenerated, hemorrhagic tumor (13 by 11 by 8 cm), arising at the tip of the diverticulum, caused torsion and complete obstruction of the ileum.

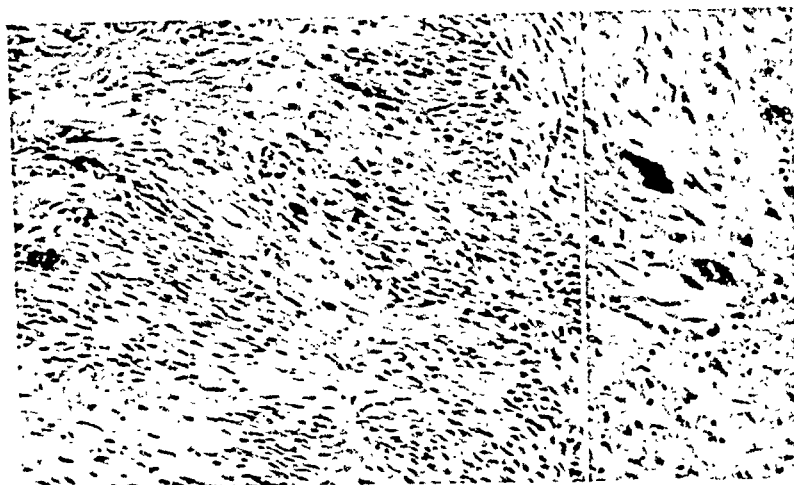


Fig. 20. Case 15. Malignant leiomyoma of Meckel's diverticulum. The cells are arranged in bundles and vary considerably in size. Some bizarre forms are enlarged at the right.

He was observed for 2 weeks and given 3 small transfusions. At the end of that time his stools were normal in color and he was discharged. During the following 4 days he again had tarry stools on two occasions and was readmitted. After 1 week there was no further evidence of intestinal hemorrhage, and he was again discharged. In the ensuing 2 weeks a barium series was reported negative, but the following week the tarry stools returned, he was again admitted to the hospital, and after a 2 week period, during which he received 6 transfusions, exploratory laparotomy was decided upon.

Operation was done by Dr. C. S. Dickson, on August 31, 1932. An ovoid, firm, elastic "hour-glass" tumor about the size of a pecan nut was found in the antimesenteric aspect of the jejunum 2 feet distal to the duodenaljejunal flexure. A 6 centimeter section of jejunum, including the tumor, was resected, followed by end-to-end anastomosis. The mass was covered by normal mucosa, except at the apex, where there was an oval ulceration 1.5 by .6 centimeters with well defined margins and evidently the site of hemorrhage. On section the cut surface presented a grayish-white, translucent sheen dotted by small hemorrhages.

Microscopically, the tumor was made up of large smooth muscle cells with elongated oval nuclei, arranged in interlaced bundles. There was some variation in size and shape, but mitoses were rare. Material for special stains was not available and myofibrils could not therefore be demonstrated. The connective tissue stroma was moderate in amount, rather vascular, and in several places there were small foci of calcification. There was no well defined capsule and at several points tongues of less well differentiated tumor tissue interdigitated with the normal muscularis (Fig. 17).

Diagnosis: Malignant leiomyoma of jejunum.

The patient made an uneventful recovery and is in excellent health 8 years following operation.

CASE 12. S. P. 66463. Unit Hist. No. 537691. A. M., a 68 year old white female admitted with a 3 months' history of sensation of weight in lower abdomen with increasing constipation. There was an abdominal mass with evidence of intestinal obstruction and an exoenteric malignant leiomyoma of the ileum was found, but could not be removed. She died 8 months after operation, 11 months after onset of symptoms. Autopsy was not permitted.

CASE 13. S. P. 68023. Unit Hist. No. 514500. S. M., a 49 year old white male was admitted with severe intestinal hemorrhage and marked secondary anemia, treated unsuccessfully over a period of 3¼ years. A 7.5 centimeter hour-glass malignant leiomyoma of the distal ileum was resected, and the patient has been in good health for 2½ years, approximately 6 years following onset of symptoms.

CASE 14. S. P. 64503. Unit Hist. No. 516225. J. L., a 30 year old white Italian male, was admitted to the Presbyterian Hospital on July 1, 1937, with a 6 months' history of left lower quadrant aching pain, gradual in onset, but constant and associated with increasing constipation.

Examination revealed moderate midline spasm and tenderness, as well as a slightly tender, firm, movable mass in the left lower quadrant. A barium series revealed only a slow emptying of the ileum.

An exploratory celiotomy on July 9, 1937, by Dr. C. L. Janssen, revealed an exoenteric, nodular tumor attached to the wall of the ileum at the junction of the middle and distal thirds. It measured 6 by 6 by 5 centimeters and on section it was grayish-pink, rubbery, and projected slightly endoenterically. There was a 2.5 centimeter central cavity with a 5



Fig 21 Case 17 Leiomyoma of descending colon The nodular tumor (0.5 by 5.5 by 5 cm) is covered by a veil of mesentery and lies behind the involved loop of bowel, which here extends from left to right. The portion overlying the tumor is flattened and widened. Cross section illustrates the glistening "watered silk" cut surface. The flattened lumen of the colon is seen at the left. The tumor is made up of well differentiated cells and myofibrils (right).



Fig 22 Case 18 Malignant leiomyoma of rectum The 4 centimeter tumor projects into the rectum and causes a slight bulge in the posterior vaginal wall, A. A cavity in the tumor due to necrosis opens into the rectum at B. The detail shows the approach of the tumor to the vaginal mucosa.

millimeter tract leading into the bowel lumen. No metastases were seen (Fig 18). A partial enterectomy with end-to-end entero-enterostomy was performed, but the patient had a stormy postoperative course. On the fourth day his wound disrupted, he went rapidly downhill, and expired the following morning. There was no autopsy.

Microscopically the poorly delimited tumor showed well differentiated smooth muscle cells in interlaced bundles, with scanty, poorly vascularized fibrous stroma. Many myofibrils were noted, mitoses were rare. Centrally, degeneration and cavitation with ulceration of overlying mucosa (Fig 18).

Diagnosis. Leiomyoma of the ileum



Fig. 23. Case 19. Malignant leiomyoma of rectum. The 5.5 by 5 by 4.5 centimeter tumor bulges forward from the posterior wall and the ulceration in the lower portion resulted from the biopsy. The inset shows the large, plump smooth muscle cells with elongated, palisaded nuclei.

#### *Meckel's Diverticulum*

CASE 15. S. P. 60740. Unit Hist. No. 244795. J. G., a 33 year old white French female was admitted to the gynecological service of the Presbyterian Hospital on April 23, 1936, for uterine bleeding following an abortion 14 weeks previously. On the day following a dilatation and curettage of the uterus, she developed acute distention, nausea, vomiting, fever, oliguria, jaundice, and a mass appeared in the left upper quadrant. There was also diffuse abdominal pain. She was transferred to the surgical service and on May 7, 1936, Dr. Rudolph Schullinger, suspecting an acute ileus due to pelvic peritonitis, did an exploratory laparotomy. He found a diverticulum of the ileum 4 feet from the ileocecal junction, covered by omentum and involved in a mass measuring 13 by 11 by 8 centimeters. This was for the most part necrotic, friable, and ecchymotic, while at the tip of the diverticulum, which was embedded in the mass, the tissue was pinkish-white and rather homogeneous. The mass had caused a torsion in the bowel, obstructing its lumen (Fig. 19) and was resected with the diverticulum and 25 centimeters of ileum, followed by a side to side ileo-ileostomy.

Microscopically, the tumor apparently originated in the muscularis of the diverticulum. It was almost entirely encapsulated by a layer of peritoneum and composed of interlaced bundles of smooth muscle cells with rather irregular, elongated nuclei and scattered myofibrils. Occasional bizarre forms were seen, but mitoses were exceedingly rare. The stroma was scanty, but highly vascularized. In many places there was hemorrhage and degeneration (Fig. 20).

Diagnosis: Malignant leiomyoma of Meckel's diverticulum.

The patient developed a pulmonary infarct with pneumonitis on the ninth day after operation and a phlebitis of the left leg on the eighteenth day, but recovered satisfactorily, and was discharged in good condition on the thirtieth day. At present, 4½ years following operation, she is alive and well, with no evidence of recurrence.

#### *Colon*

CASE 16. P. & S. 15225. Army Medical Museum No. 54461. Sections of a malignant leiomyoma of



Fig. 24. Case 31. Leiomyoma of stomach. The section illustrates a striking resemblance to a neurilemmoma. The closely packed, palisaded nuclei are interspersed with areas of loosely arranged, degenerated stroma, thus imitating the differentiation into A and B tissue of a neurilemmoma. The myofibrils in this tumor indicated smooth muscle origin.



Fig. 25 Case 32 Leiomyoma of stomach. This was an incidental finding in a stomach resected for duodenal ulcer. It lies entirely within the external layer of muscle with which it interdigitates.

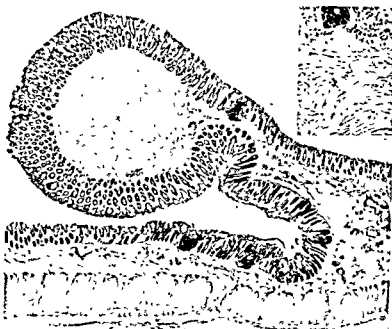


Fig. 26 Case 36 Pedunculated leiomyoma of sigmoid colon. The 15 by 15 millimeter tumor lies in the submucosa in continuity with the muscularis mucosae and entirely separated from the muscularis. The detail shows its well differentiated cells and myofibrils.

the sigmoid colon were submitted by Major Elbert DeCoursey, M. C.

The patient was a 78 year old white male who had an abdominal mass and slight intestinal hemorrhage for 6 months. The tumor was about the size of a 6 months' fetus and 1 year after its removal his condition was entirely satisfactory.

CASE 17. S. P. 62450. Unit Hist. No. 503207. H. F., a 47 year old white American female was admitted to the Presbyterian Hospital on November 11, 1936, complaining of intermittent severe attacks of cramping left lower quadrant pain of 4 years' duration, coming on every 6 to 8 weeks and lasting 24 hours. They were associated with nausea, vomiting, and constipation, alternating with obstipation.

Examination revealed a firm, tender, deep, immoveable orange-sized mass high in the left lower quadrant. A barium series, done elsewhere, revealed an "extra loop of bowel."

At operation, on November 16, 1936, Dr. Allen O. Whipple found a nodular, exocolonic tumor partially obstructing the lumen of the descending colon. It was kidney-shaped, measured 0.5 by 5.5 by 5 centimeters, and on section presented a rubbery, semitranslucent, pinkish-white, glistening "watered-silk" cut surface. There was no evidence of metastases. The lumen of the bowel in this region was markedly flattened and widened, while the uninvolved portion was somewhat narrowed (Fig. 21). The mass, with 0.5 centimeters of large bowel, was resected, followed by end-to-end anastomosis.

Microscopically, the tumor was made up of well differentiated smooth muscle tissue with abundant fibrous stroma. It was well circumscribed, lying just beneath the muscularis mucosae. Numerous myofibrils were seen and there were no mitoses (Fig. 21).

Diagnosis: Leiomyoma of descending colon. Convalescence was uneventful and at present, 4 years after operation and 8 years after onset of symptoms, the patient is in good condition, showing no evidence of recurrence.

#### Rectum

CASE 18. S. P. 65922; 66089; 74004. Unit Hist. No. 538227. M. R., a 51 year old white American female was admitted to the Presbyterian Hospital on December 20, 1937, with a history of rectal bleeding, tenesmus, and much gas for 2 weeks. The bleeding was quite marked and resulted finally in extreme weakness.

Examination revealed a moderate anemia and a well defined tumor mass in the lower rectum. It was pale pink, finely lobulated and measured 4 centimeters in diameter. The overlying mucosa was ulcerated, and there was central cavitation. The mass bulged slightly into the rectal lumen and extended into the posterior wall of the vagina, but was without mucosal involvement.

Several small pieces of tissue were passed spontaneously and examination of these revealed whorled masses of closely packed, large spindle shaped cells arranged in interlaced bundles. The nuclei were

elongated, blunt-ended, and varied somewhat in size and shape. Occasional mitoses were noted, but no myofibrils could be demonstrated.

A diagnosis of malignant leiomyoma of the rectum was made and on January 13, 1938, Dr. C. L. Janssen removed the mass (Fig. 22) by wide excision involving a partial colectomy and proctectomy with establishment of a permanent colostomy.

Microscopic sections (Fig. 22) were similar to the previous ones. The tumor was rather well preserved and sharply circumscribed, except at the proximal cut edge. Here, there was an area of extension outside of the main tumor mass alongside of a vein and it was feared that this might be responsible for reappearance of the tumor. The vaginal mucosa was closely approached, but no invasion was seen.

The patient's convalescence was uneventful, and she was discharged in good condition, but within several months there was a recurrent nodule measuring 1.75 centimeters in diameter in the operative site. This was widely excised on April 18, 1940, 2 years after the first operation, and proved to be similar to, but less well preserved than, the original tumor. At present, 8 months after the last excision, and 3 years following the onset of symptoms, she is well, showing no evidence of further recurrence.

CASE 10. S. P. 74371; 74404. Unit Hist. No. 610051. E. J., a 59 year old white American male was admitted to the Presbyterian Hospital on May 10, 1940, complaining of sacral pain and a mass in the rectum of 1 year's duration. The stool had decreased in caliber in the last 2 to 3 months and he had lost 18 pounds in weight, but explained the latter on the basis of severe grief for his wife's recent death. The pain began at the base of the spine and radiated to the left hip and knee.

Examination revealed a firm, non-tender rectal mass measuring 5.5 by 5 by 4.5 centimeters. It was situated just above the crypts of Morgagni in the posterior wall, and bulged into the lumen about 2.5 centimeters. The overlying mucosa was flattened but intact. Just below the mass there was a 2 centimeter external hemorrhoid and another smaller one was seen in the anterior midline (Fig. 23). A diagnosis of malignant leiomyoma of the rectum was made and substantiated by biopsy, taken on the day after admission.

On May 14, 1940, a colostomy with perineal proctectomy was performed by Dr. C. L. Janssen and recovery was uneventful.

Microscopic sections of the tumor showed interlaced bundles of large, plump smooth muscle cells, with elongated palisaded nuclei. Myofibrils were seen occasionally and no mitoses were noted. The fibrous stroma was scanty, relatively avascular and the overlying mucosa was intact (Fig. 23).

Diagnosis: Malignant leiomyoma of the rectum. The patient is in excellent health at present, 6 months after operation and 1½ years following onset of symptoms. There is no evidence of recurrence, but the elapsed time since operation is still too short for adequate evaluation of his course.



CASE 20. S. P. 46846; 48387. Unit Hist. No. 318864. Autopsy No. 10970. A. S., a 64 year old white male was admitted with a rectal tumor of 3 years' duration. No hemorrhage. He died 2 days after a preliminary colostomy was performed and autopsy showed an exorectal malignant leiomyoma 11 centimeters in diameter. Death was caused by a marked urinary infection.

CASE 21. P. & S. 7872. (Courtesy of Dr. William Brandes, Roosevelt Hospital). W. P., a 61 year old white Scotch male, was admitted to Roosevelt Hospital on July 30, 1922, complaining of a rectal mass. It began as a small growth 8 months previously and had grown rapidly, attaining the size of a plum. It protruded during defecation and caused urgency and constipation. His general health was satisfactory. The tumor was attached by a 2.5 by 1 centimeter pedicle to the left lateral aspect of the rectum and measured 6 centimeters in diameter. It was irregular, indurated, and partially covered by a necrotic, greenish-gray membrane. Opposite this mass were several small, hard, sessile nodules, each about the size of a large black-headed pin.

On July 22, 1922, under a diagnosis of "polypoid tumor of rectum," Dr. J. I. Russell excised the mass through its pedicle. The other nodules were noted, but not treated, and were to be observed periodically.

Microscopically, the tumor was composed of interlaced bundles of rather well differentiated smooth cells in a scanty fibrous stroma, showing a moderate amount of degeneration. Occasional mitoses were seen and there was variation in cellular size and shape. Special stains for demonstrating myofibrils were not available.

Diagnosis Malignant leiomyoma of rectum.

Patient was discharged in good condition on the ninth day after operation, but he was lost to follow-up after his discharge and it is not possible to comment on his subsequent course or the fate of the rectal nodules which were not removed.

CASE 22. S. P. 50748. Unit Hist. No. 366781. Autopsy No. 11628. A. W., a 67 year old white male was admitted with symptoms of an enlarged prostate. During prostatectomy a 5 centimeter leiomyoma of the rectum was also found and enucleated. One and one half years later he died of chronic bronchitis with bronchiectasis.

#### *Retropertoneal Tissues and Mesentery*

CASE 23. S. P. 54932. Unit Hist. No. 421725. L. E., a 39 year old white female was admitted for treatment of abdominal swelling, weakness, and epigastric pain, present for 2 years. A retropertoneal malignant leiomyoma with metastases to the liver was found and a biopsy specimen only removed. When last heard from, 6 months after operation, she was bedridden, and death appeared imminent.

CASE 24. S. P. 40011. Unit Hist. No. 79613. E. T., a 57 year old white American female was admitted to the Presbyterian Hospital on March 12, 1929 with a 5 year history of loss of appetite and strength, together with a weight loss of 59 pounds.

Two years previously she began to have attacks of cramp-like abdominal pains accompanied by gaseous eructations and bloating. Pain radiated to the umbilicus and flanks and was most severe in right lower quadrant. There was marked constipation. Symptoms increased in severity in past few months and were accompanied by distention.

Examination revealed a hard, firm, nodular mass in the medial aspect of the right lower quadrant. There was moderate anemia. A barium series showed a partially calcified abdominal mass and diverticulosis of descending colon and sigmoid.

On March 12, 1929, Dr. William Barclay Parsons excised this mass. It was firm, lobulated, and measured 12 by 8 by 6 centimeters, apparently originating in retroperitoneal tissue in the right lumbar region. The right ureter was encircled between two lobules of the tumor. The cut surface was gray, partially translucent, and more or less uniform.

Microscopic examination revealed interlaced strands of uniform smooth muscle cells in which myofibrils could be identified. Mitoses were rare. The relatively avascular stroma was scanty and many large areas of degeneration were noted.

Diagnosis. Leiomyoma of retroperitoneal tissue. Recovery was uneventful and patient gained 50 pounds in the following year. For 4 years her condition remained good, then her symptoms returned. She returned to the hospital and the genitourinary service found a recurrent mass attached to the lower pole of the right kidney, as well as the psoas fascia and scar of previous operation. On November 3, 1933, Dr. George Cahill removed the kidney with the mass, but the kidney contained no tumor tissue. The tumor closely resembled the original. About 3 months later, on January 20, 1934, Dr. Parsons explored her again and found marked extension into and around the terminal aorta with numerous metastatic nodules in the liver. A biopsy (S. P. 53298) taken at that time revealed no further evidence of malignancy, but in view of the rapid recurrence and metastases the final diagnosis had to be changed to malignant leiomyoma of retroperitoneal tissue with metastases to liver.

Patient went steadily downhill and expired December 11, 1934, 5½ years after the first operation and 10½ years after onset of symptoms. No autopsy could be obtained.

CASE 25. S. P. 69790. Unit Hist. No. 570124. J. D., a 60 year old white female was admitted with a 4 year history of a left-sided, slowly growing abdominal mass. A retropertoneal, malignant leiomyoma with metastases to the peritoneum was found and biopsied only. The tumor grew rapidly following the operation and she expired 1 month later. An autopsy could not be obtained.

CASE 26. S. P. 35101. Unit Hist. No. 66636. Autopsy No. 9838. H. P., a 70 year old white male was admitted with symptoms of enlarged prostate for 5 years. During prostatectomy a retropertoneal malignant leiomyoma was also found. An attempt at removal was made 1½ months later, but he ex-

pired 4 hours after this second operation. Autopsy revealed a gangrenous cystitis.

CASE 27. P. & S. 17470. M. S., a 66 year old white female had recurrence of a retroperitoneal malignant leiomyoma which had been excised 5 years ago. The tumor was again removed, but only incompletely, and within 3 months of the second operation there was another recurrence. At present, 6 years after the first operation and 9 months after the second, she is failing rapidly.

CASE 28. S. P. 58557. Unit Hist. No. 463624-A. C., a 52 year old white female was admitted with a 1 year's history of intermittent left upper quadrant abdominal pain and a mass. A retroperitoneal malignant leiomyoma was found, but could only be biopsied. She died 24 hours after operation of an undetermined cause. No autopsy.

CASE 29. Unit Hist. No. 35248 (Neurological Institute). Autopsy No. 12641. R. Z., a 32 year old white American male was admitted to the Neurological Institute on October 4, 1937, complaining of pain in left lumbar region, constipation, impotence, weakness of both lower extremities and lower abdominal muscles and swelling of feet and legs for eight months. There were also bladder disturbances. In September he had had a spinal tap in Arizona, following which he became unable to make use of his lower extremities.

Examination revealed almost complete paraplegia of the lower extremities with loss of sensation up to first lumbar on the right and eleventh thoracic on the left. There was edema of the feet and ankles, marked atrophy, and severe sacral decubitus with lesser ulcerations on both hips. Temperature ranged from 99 to 104 degrees F. Roentgenogram findings were strongly suggestive of an extradural sarcoma involving twelfth thoracic and first lumbar vertebrae. Patient was treated by roentgenotherapy, but developed a pyelonephritis, became comatose, and expired December 17, 1937, 10 months following onset of symptoms.

At autopsy, a large lobulated tumor mass was found in the left retroperitoneal region, firmly attached to, and invading the left psoas muscle, as well as the first, second, and third lumbar vertebrae. There was a curious extension into the inferior vena cava by an isthmus of tumor tissue across the vertebrae and projecting into the vena cava. It apparently did not completely obstruct the lumen. On section, a firm whitish, whorled cut surface was seen. Microscopically, the tumor was made up of well differentiated, uniform, interlaced smooth muscle cells containing palisaded elongated nuclei. Numerous myofibrils were present and mitoses were rare. There was a moderate amount of fibrous stroma.

Diagnosis: Leiomyoma of retroperitoneal tissue. CASE 30. S. P. 52994. Unit Hist. No. 398006. R. M., a 44 year old white Irish female was admitted to the gynecological service of the Presbyterian Hospital complaining of vaginal bleeding for 27 days, and a fixed, circumscribed, slightly tender mass in the right lower quadrant for six months.

Examination revealed that the mass extended from the umbilicus to the pelvis. Cystoscopy and roentgenography showed a right hydronephrosis due to a mass extrinsic to the gastrointestinal tract.

On December 12, 1933, following dilatation and curettement of the uterus, Dr. Allen O. Whipple found an indurated, fibrous mass involving a large portion of the mesentery of the ileum and the ileocolic vessels. It measured 10 by 8 centimeters, and the transverse colon was adherent to it. It bled easily and was considered inoperable, so that only a biopsy was taken.

The biopsy specimen was composed of a few well differentiated smooth muscle cells in an abundance of poorly vascularized connective tissue stroma. The cells were quite uniform and myofibrils were rare, but no mitoses were seen.

Diagnosis: Leiomyoma of mesentery of ileum. The patient made a satisfactory recovery and it was decided to try roentgenotherapy on the mass, but it apparently decreased in size somewhat, much to the surprise of observers, and treatment was refused by the patient. Her condition continued satisfactory and at present, 7½ years after appearance of the mass, she is in good health, employed as a domestic. The tumor appears definitely smaller, and remains entirely symptomless.

## SUMMARY

1. Smooth muscle tumors occur throughout the entire gastrointestinal tract and often in the retroperitoneal tissues. They are found most commonly in the stomach and their incidence in general is much higher than suspected.

2. Classification of the tumors into benign and malignant is difficult because frequently poorly differentiated ones, which have the histological criteria of malignancy, do not display its clinical evidences, while occasionally a well differentiated tumor has grown by infiltration and metastasized. The terms leiomyoma and malignant leiomyoma are preferred to any others proposed. However, such classification has not been based solely upon histological criteria, but has been modified occasionally by biological behavior.

3. Early diagnosis is seldom accomplished, but if the possibility of such a tumor is kept in mind, more of these cases will be benefited by early treatment before secondary complications determine a less favorable prognosis. The presence of this type of tumor should be suspected, especially in all cases of gastrointestinal hemorrhage if the origin has not been determined.

4. Surgery is the only method of treatment and in many instances must be of a radical nature.

5. Prognosis is as much dependent upon the anatomical site of the tumor as upon its histological character. Tumors of the stomach, jejunum, ileum, and colon are restrained for a long time by the barrier of the peritoneum so that they can be entirely removed, usually with success. The anatomical peculiarities of the duodenum, the rectum, and the retroperitoneum make the complete removal of their tumors more difficult and sometimes impossible. For this reason recurrence following attempted surgical removal has been more frequent and the prognosis therefore much less favorable.

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# DYSGERMINOMA OCCURRING IN A PSEUDOHERMAPHRODITE

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PRIOR to the important work of Robert Meyer in rationalizing the classification of ovarian neoplasms, numerous confusing terms were applied to the new-growth known at present as dysgerminoma ovarii. Because of variations in its histological structure, this tumor had been described variously by pathologists and clinicians as embryonal carcinoma, carcinosarcomatodes, giant cell sarcoma, embryoma, alveolar large cell carcinoma, and round cell sarcoma. It was reported in the female first by M. Chenot who, in 1911, described an ovarian tumor which he called "seminoma," because he thought it was derived from the anlage of seminiferous tubules. A year later, Pick reported the same tumor as "chorioepithelioma ectodermale" and postulated that it was derived from cells of chorionic villi. In 1931, Robert Meyer wrote that he had begun collecting cases "a long time ago," and had found 27 examples in hermaphrodites and pseudohermaphrodites, and 21 in otherwise normal females. It was his important observation, that this and others of the ovarian tumors have definite relationship to the hormonal activity of the gonads, which gave new impetus to the study of ovarian neoplasms. He rejected the name "seminoma" because there is no tendency toward masculinization, and suggested the term "dysgerminoma" because of the frequent appearance of the tumor in pseudohermaphrodites and in female subjects with poorly developed genitalia.

## HISTOGENESIS

Following Meyer's effort to classify tumors of the ovary on the basis of their hormonal effect, other investigators studied more carefully the histogenesis of the ovary in an attempt to correlate the new clinical concepts with the morphological findings in the developing gonad. Ewing and Meigs, among others, developed the concept that dysgerminoma represents a one-sided development of a plasm springs from sexually undifferentiated cells developed from the surface epithelium of the anlage of the ovary. Schattenberg and Harris (17, 18), Chaney and Greenblatt, Novak and Gray, together with Meyer believed that dysgerminomas arise from cell rests, which are left over from that stage in gonadal development in which there is no sexual differentiation and which subsequently lose their faculty of becoming either masculine or feminine in type. In his recent excellent paper, Schiller (20) expressed the opinion that these tumors originate by reason of an error in differentiation of the mesenchymal core of the developing ovary. According to this explanation, the mesenchyme of the primitive gonad is undifferentiated when invaded by germinal cells from the primordial gut. Instead of normal development into Sertoli cells or granulosa cells of the normal testicle or ovary, the mesenchyme, by chromosomal malformation, may be transformed into neutral cells which remain as fetal remnants, later to develop into a sexually nonspecific neoplasm. In his classification, Schiller is able thus to place dysgerminomas in the group of ovarian tumors arising from tissue not normally found in the female gonad but present because of cellular malformation of the mesenchymal core into nonspecific interstitial tissue. Seegar's opinion that the histogenesis of dysgerminomas is not established is supported by Ewing's recent statement that "the embryology of the ovary is highly obscure."

Part of the increased interest in ovarian neoplasms stimulated by Meyer's work has been

indicated by the re-examination by various investigators of old records and specimens in an effort to reclassify solid ovarian tumors according to the new terminology. Thus Meigs (11, 12) in studying histologically the ovarian tumors found at Massachusetts General Hospital between the years 1924-1935 discovered 5 cases of dysgerminoma; Russell found 7 such tumors after an examination of the specimens of 30 years at University College Hospital School (London); 3 cases were found in the Gynecological Museum of the Long Island College of Medicine by Wolfe and Kaminister; Seegar in 1938 collected 79 cases of dysgerminomas from the literature and added 19 more found among the pathological specimens at Johns Hopkins. In an analysis of 400 solid ovarian tumors removed surgically at the Mayo Clinic, Dockerty found 9 instances of dysgerminoma, or an incidence of 2.25 per cent; Klaften in a similar survey at Universitaets Frauenklinik in Vienna found an incidence of 3 per cent in 188 solid ovarian tumors. We have attempted a like investigation at Charity Hospital of Louisiana at New Orleans, covering the period 1932 to 1940, but among a group of 68 solid ovarian tumors found at operation and at autopsy, we have discovered only one dysgerminoma, that being the case which first initiated this study and which is herewith reported. Other results of our investigation will be reported in a subsequent communication.

#### CLINICAL CHARACTERISTICS

In the renaissance of interest in ovarian neoplasms an early observation was the high incidence of dysgerminomas among pseudohermaphrodites and in women with poorly developed genitalia. In the former group it is said to be the most common new-growth. The preponderance of pseudohermaphrodites in Meyer's series has already been alluded to. Of 64 cases reported by Fauvet, 27 were in pseudohermaphrodites and 2 were in true hermaphrodites. Of Seegar's collected series of 79 cases, only 50 were otherwise normal individuals, and of his 19 personal cases, 15 had normal external genitalia and secondary sex characteristics. Reported indications of low sexual potential in patients other than

pseudohermaphrodites are such common symptoms as amenorrhea, delayed onset of menses, sterility, asthenia, oligomenorrhea, dysmenorrhea; the tumor with genital hypoplasia, infantilism, or with functionally inefficient gonads and breast hypoplasia occurs frequently.

It is generally agreed that dysgerminomas elaborate no specific hormone. The few biological assays which have been made have been inconclusively negative. Spielman and Morton reported the first study of extracts of the tumor for estrogenic and gonadotropic hormones and in this a weakly positive result was obtained for the latter hormone. Since an increase in gonadotropic or pituitary-like hormone has been observed repeatedly in amenorrheic females, no conclusions were drawn. These authors summarize the inconclusive results of the biological investigation of the urine by Wallis, Kleine, and Fauvet, and comment upon the paucity of data in this field. Seegar speaks of Zondek's assays of tumor and urine as also negative in result.

Although the consensus seems to be that the relation of dysgerminomas and female hypogonadism is coincidental and not causative, this conception by no means is universal. In writing of dysgerminoma, Meigs (12) states, "Its hormone is potent enough to prevent proper female development in some cases." Greenblatt and Pund hold much the same opinion. One of the Johns Hopkins cases was a female pseudohermaphrodite who, following the removal of a dysgerminoma from the left broad ligament, had a regression of male characteristics. A most interesting case is reported by Gough; that of a broad shouldered, muscular girl of 15 years who had a deep voice, male distribution of hair on body and face, and male habits. Following the removal of a large dysgerminoma there was a partial retrogression of these male attributes. Gough believes that in his patient the tumor elaborated abundant male hormone which inhibited the growth of the other ovary and caused the secondary male sex characteristics. He further suggests that in this group of patients normal female sexual development occurs only in those women in whom the tumor has arisen following the appearance of feminine characteristics.

A large pelvic tumor in a pseudohermaphrodite or in a female with infantile genitalia suggests dysgerminoma, but the diagnosis is not so easily made in those women who have normal secondary sex characteristics. Aside from symptoms referable to a disturbance of hormonal balance, the complaints and findings are usually those due to a large and rapidly growing pelvic tumor. Changes in the menstrual period, abdominal pain and enlargement are the common complaints. The tumor as a rule enlarges rapidly, attaining a size sufficient to fill the lower abdomen in 3 to 6 months. Degeneration of the fast growing mass frequently occurs and is sometimes responsible for fever, night sweats, and leucocytosis up to 20,000 cells per cubic millimeter. Other more infrequent symptoms, some of which are due to pressure, others to malignant extension, are renal colic, urinary frequency, respiratory embarrassment, diarrhea, vomiting, ascites, anemia, and loss of weight. The tumor is one of childhood and young adulthood, frequently having its onset early in puberty. Novak and Gray report its occurrence in a woman of 52 years, but more than 70 per cent of the tumors are said to appear before the age of 30 years (Dockerty and Seegar). In this characteristic it varies widely from its homologue, the testicular seminoma, which rarely is found before the thirtieth year.

The diagnosis rests largely upon a consideration of the duration of symptoms, the age of the patient, state of sexual development, and the presence of a rapidly growing pelvic neoplasm. Palpation of the abdomen and pelvic examination reveal a hard, elastic mass with an irregular, nodular surface. Occasionally the x-ray may be able to differentiate a teratoma or dermoid cyst from a dysgerminoma by demonstrating the presence of calcium in the tumor.

Opinions as to the incidence of malignancy in dysgerminomas vary all the way from that of Schiller (19, 20) in whose experience 70 to 90 per cent, and practically all unilateral tumors, were benign, to that of Wolfe and Kaminister and Greenblatt and Pund whose small series of 3 and 5 cases, respectively, all proved malignant. As yet there are such few cases on record and each writer's experience is

so small that no clear conception of the degree of malignancy has been gained. The pathologist is able to add little to the problem's solution, for, histologically, all dysgerminomas display malignant features, and there appears to be no constant relation between these and the degree of malignancy. At present the most valuable criteria of the malignancy of individual tumors are clinical. If at operation a unilateral tumor is found which has no obvious extension, as indicated by the absence of infiltration of adjacent structures and regional lymph node involvement, it may be regarded as benign until proved otherwise by the clinical course. Infiltration of the broad ligament, uterus, opposite ovary, rectum and bladder, and lymphatic spread to the retroperitoneal lymph nodes occur in a definite proportion of cases, but metastases to distant organs are rare. Seegar was able to find only 2 such instances in the literature, one case in which there was metastatic involvement of the kidney and another case which spread to the liver; he added from his series one case of metastasis to the spleen, kidney, and pancreas. When extension has occurred there is a poor ultimate prognosis. However, the more efficient utilization of x-ray therapy may alter this situation since dysgerminomas seem to be affected by irradiation much like the lymphomas, being much more radiosensitive than the identical tumor in the testicle.

The importance of accuracy in estimating the degree of clinical malignancy at the time of operation is self-evident when the occurrence of dysgerminomas in young individuals is placed in relation to the effective methods of treatment of the malignant phase, viz., radical surgery and deep x-ray therapy. The price paid by the patient for this form of treatment is removal or destruction of both ovaries. While this fate is of little concern to the pseudohermaphrodite or to the patient with marked hypogonadism, it is greatly undesired by the young girl who has not yet developed secondary sex characteristics and by the young woman who desires to bear children. Seegar could find reported only 2 instances in which the opposite ovary showed neoplastic change after the removal of a dysgerminoma, but numerous reports are in the literature of

pregnancy ensuing following the operative removal of the tumor alone.

Simple extirpation has come to be considered good judgment on the part of the surgeon who finds at operation a solid, non-adherent, ovarian tumor. Should gross and histological study prove the mass to be a dysgerminoma, frequent follow-up examinations should be made in an effort to discover early any possible recurrence of the neoplasm, which when found should then be treated by irradiation. If, on the other hand, there is present at operation evidence of local extension, a more radical surgical procedure should be adopted and followed after operation by deep x-ray therapy. In inoperable cases, thorough irradiation alone remains the treatment of choice. Those patients whose advanced dysgerminomas are attacked early are offered an excellent prognosis.

#### **PATHOLOGICAL CHARACTERISTICS**

Dysgerminomas are bilateral in 20 to 35 per cent of cases (Dockerty and Schattenberg, 17, 18). They are usually comparatively large when seen by the pathologist, frequently being described as the "size of an adult head." The tumor mass is usually lobulated and frequently peculiarly kidney shaped. Over the smooth encapsulated surface run numerous dilated veins. Adhesions are essentially absent unless the capsule is perforated by malignant extension of the neoplasm, in which instance there may be an infiltration and adherence to any of the adjacent pelvic structures. The opposite gonad, normal or undeveloped, may be so completely replaced by tumor as to make sex determination impossible (Geist). The tumor is usually of a firm but elastic or doughy consistency.

The cut section presents a homogeneous, friable, glistening, brain-like surface through which run scanty fibrous septa. Areas of yellowish discoloration indicate lipoid degeneration, and frequently this has progressed to the stage of frank necrosis with the formation of broad zones of necrotic tissue and hemorrhagic cysts of varying size.

The microscopic appearance of sections of dysgerminoma is one of the most characteristic found among solid ovarian tumors. The

tumor cells are large and round with hyperchromatic centrally placed nuclei containing large nucleoli, and a narrow lightly granular cytoplasm. Frequent mitotic figures appear. The cells are loosely arranged in columns or islands, frequently described as alveolar, separated by varying amounts of loose, edematous, poorly vascularized connective tissue. Degenerative changes and hemorrhages are common. The connective tissue nearly always is diffusely infiltrated with lymphocytes, and these with the presence of small epithelioid cells and large giant cells create a picture simulating tuberculosis. However, as Schiller (19, 20) points out, the giant cells do not lie in the center of the focus, as in tuberculosis, but often outside and even isolated between tumor cells. He suggests that there is a lipoid substance created by the necrosis of dysgerminoma cells which causes a tissue reaction similar to that stimulated by tuberculin. It would appear that much of the connective tissue in these sections is replacing areas of tumor necrosis and that the lymphocytic infiltration is a part of the same process. The entire histological picture is one of an undifferentiated, highly malignant neoplasm which closely approximates that found in seminoma of the testicle. A dysgerminoma in which there is scant stroma and in which the lymphocytic infiltration is not a prominent feature is easily confused with large round cell sarcoma.

**CASE REPORT.** A white man, of 21 years, was admitted to the Tulane Surgical Service of Charity Hospital on July 27, 1932, complaining of severe lower abdominal pain which had been present for 2 days. He had always been in good health and had never consulted a physician previously.

On close questioning he gave the following interesting history. From early childhood he had been shielded by his parents from the prying eyes of his brothers and sisters because of his abnormal external genitalia. He knew little about these except that his penis was small and that he urinated from a opening behind it. At the age of 13 there was a marked deepening of his voice and he began to have penile erections. He was always popular with the girls and went out a great deal with them. He stated that he had a "lot of passion" and that his penis remained erect for long periods of time after the slightest contact with a female. He found it necessary to have once weekly. He had never menstruated.

Physical examination revealed him to be a slender young man of moderate height who was intelligent

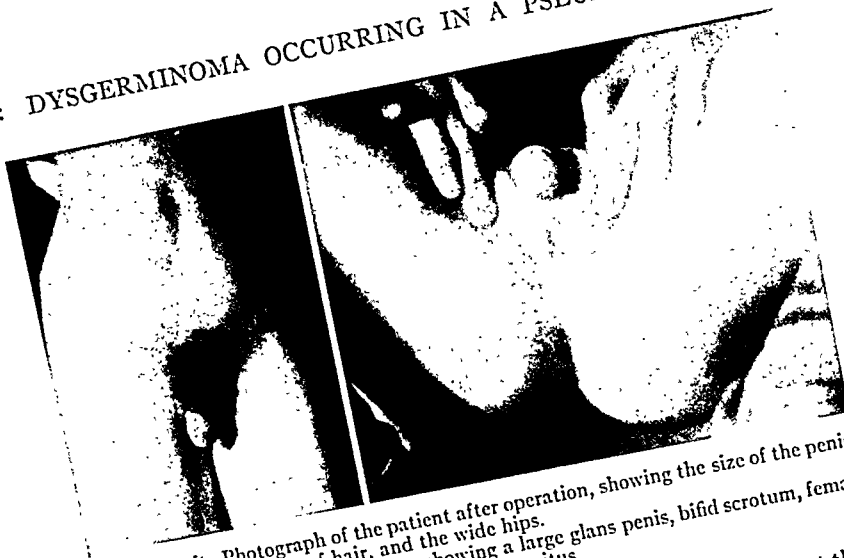


Fig. 1, left. Photograph of the patient after operation, showing the size of the penis, the female distribution of hair, and the wide hips.  
Fig. 2. Photograph of the patient showing a large glans penis, bifid scrotum, female urethral orifice behind which is the vaginal introitus.

and co-operative. The general impression which he gave was that of a boy several years younger than the stated age. He spoke in a low voice. The shoulders were narrow and the hips comparatively wide. The breasts were male in configuration, but there was a female distribution of pubic hair. The abdomen contained a firm mass filling the left lower quadrant, and in this same region there was marked tenderness and rigidity of the abdominal muscles.

The diameter of the penis was within normal limits, but there was a third degree hypospadias, and the penis was bound down by its frenulum so that it could not be lifted up in a position normally assumed during erection. Testicles could not be found. Instead of a scrotum there were present what appeared to be well defined labia majora. The urethral orifice was found between the bifid scrotum or labia at the base of the penis; just posterior to it was a vagina which appeared as a second opening, slightly larger, running internally to a small cervix uteri. On digital rectal examination, a small mass was palpated which was thought to be an infantile uterus; there was no evidence of a prostate. X-ray plates made after lipiodol injections of the vagina demonstrated a well formed canal which deviated to the right because of the left-sided tumor.

A clinical diagnosis of teratoma and hermaphroditism was made.

On August 7, 1937, laparotomy was performed by one of us. In the peritoneal cavity was a liter of xanthochromic fluid. A tumor the size of a large grapefruit was found protruding from the left side of the pelvis; it was twisted on its pedicle and some recent hemorrhage was observed beneath the capsule. This mass was apparently a neoplastic ovary. The opposite ovary was small, and the uterus and tubes were rudimentary. An unsuccessful search was made for testicles. After a bilateral salpingo-oophorectomy, the patient recovered in due course.

The pathologist reported that the tumor measured 19 by 11 by 8 centimeters. It was kidney-shaped, fairly firm in consistency, and had apparently an elongated, broad pedicle. The external surface was lobulated, and beneath the capsule could be seen several cystic areas. The opposite ovary measured 1 centimeter in diameter and was firm in consistency and white in color. On its surface was a small verrucous projection 2 millimeters in diameter. The attached fallopian tube measured 3 by 0.5 centimeters. The microscopic picture of the tumor was typically that of dysgerminoma. Sections of the opposite gonad showed that it too was the seat of similar neoplastic growth, in which were found small localized deposits of calcium. A nodule projecting from the

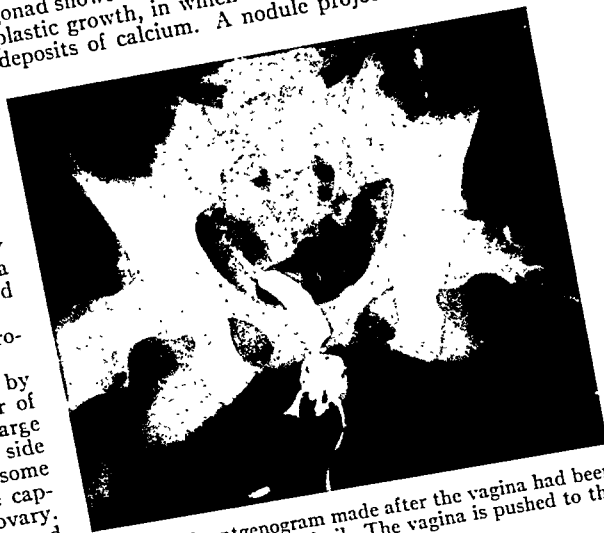


Fig. 3. Roentgenogram made after the vagina had been distended with iodinated oil. The vagina is pushed to the right by the large tumor.





Fig 4 Drawing showing the large lobulated left ovarian tumor and the small right ovary and fallopian tube, with minute secondary neoplastic deposits on the surface of the ovary.

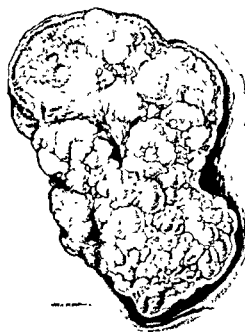


Fig 5 Cut surface of the primary tumor, showing its lobular structure and areas of necrosis and hemorrhage

surface of the smaller ovary consisted of tumor tissue in which there were many calcified areas

The patient was readmitted on April 7, 1938, at which time there was no evidence of recurrence of the dysgerminoma. A first stage plastic operation was performed for the correction of the hypospadias. The patient was discharged with instructions to return in one month, however, he decided to retain his deformity rather than submit himself for further plastic procedures.

The patient was last seen on June 15, 1940, and at this time a thorough examination revealed no evidences of recurrence. He stated that he was in excellent health, had gained 20 pounds in weight since his operation, and was employed regularly. During the first 6 months following the removal of the tumor he had no penile erection, afterward, however, there were occasional morning occurrences. He was married 13 months before this interview, and although he has an erection and attempts sexual relations 3 or 4 times weekly, he has never been able to consummate intercourse because of the inability of the penis to assume a normal position during erection. On these occasions the penile engorgement gradually disappears after 30 or 45 minutes without a definite orgasm and without ejaculation. Neither is there discharge from the vaginal orifice at any time. This state of conjugal frustration seems to be quite satisfactory to both parties, for the patient reiterated his complete marital happiness and firmly refused to undergo further plastic procedures.

Our patient has been called a female pseudohermaphrodite because we have been

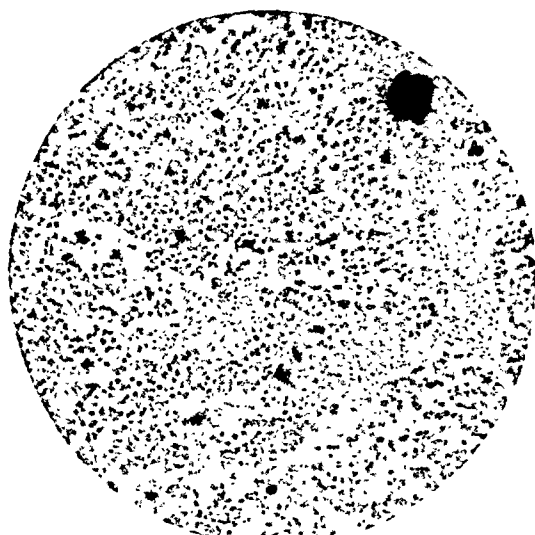


Fig. 6.

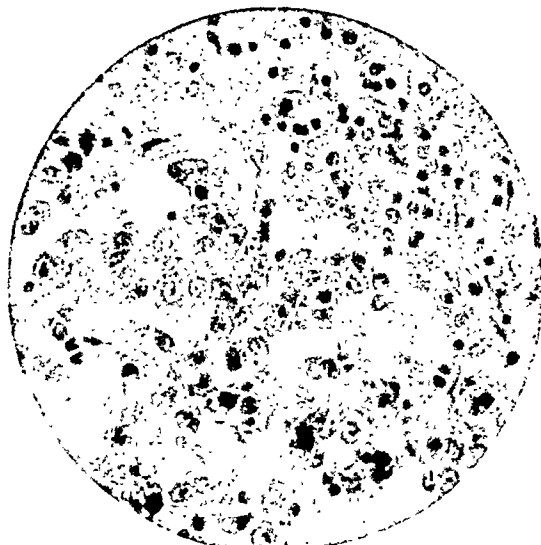


Fig. 7.

Fig. 6. Typical section of left ovarian tumor, composed of rather loosely arranged large round cells, with a scanty supporting stroma infiltrated by lymphocytes.

Fig. 7. High power view of section from left ovarian tumor showing more in detail the cells with their large hyperchromatic nuclei and the scanty supporting stroma infiltrated with lymphocytes. A tendency to formation of acini is evident.

Fig. 8. Low power view of section taken from right ovary, showing normal ovarian cortex beneath which lies neoplastic tissue surrounding a large deposit of calcium.

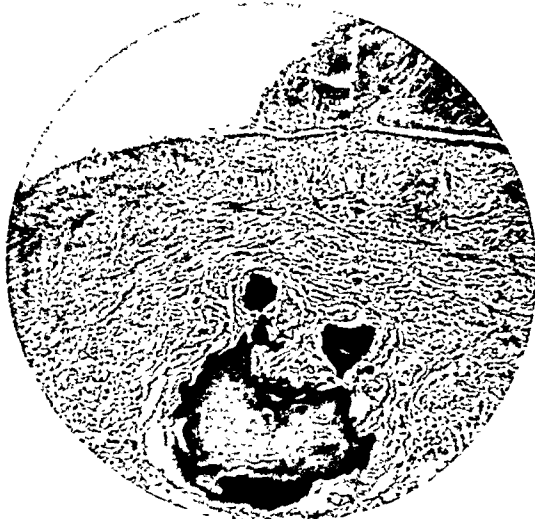


Fig. 8.

unable to demonstrate histologically both ovarian and testicular tissue and thus qualify him as a true hermaphrodite, a condition which Huggins, Cohen, and Harden could find reported in the literature only 15 times. The male characteristics can be explained by one of two assumptions: he may be a true hermaphrodite with testicles which we were unable to find; or this ovarian tumor may have elaborated the male sexual hormone.

That the latter possibility may have been the case is suggested by the temporary diminution in sexual powers following the removal of the tumor, but is discredited by the subsequent development of a masculine sex urge.

#### SUMMARY

1. Dysgerminoma is a potentially malignant tumor which has its origin in the mesenchymal core of the ovary.

2. It occurs infrequently during the first three decades of life, most characteristically appearing in women with malformed or poorly developed genitalia.

3. Although generally considered without hormonal effect, it may have some inhibitory influence upon normal female physiology.

4. Gross pathological characteristics are its firm consistency, comparatively large size, and the homogeneous brain-like appearance of its cut surface. Microscopic sections show large round cells, which stand out distinctly, and scanty stroma infiltrated by lymphocytes.

5. Local extension is not uncommon, but metastasis to distant organs is rare.

6. Surgical removal, followed by irradiation in those cases with metastatic extension, is usually effective in the treatment of these tumors.

7. An example of this unusual tumor occurring in both ovaries of a pseudohermaphrodite is reported.

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# USE OF SYNTHETIC, NONABSORBABLE SUTURE MATERIAL IN SURGERY

## Preliminary Report

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**D**URING the past few years there has been a distinctly increased tendency to use nonabsorbable material for sutures and ligatures (1-4, 6-10, 13, 14, 16, 17). The time-honored catgut has its enemies but so does the silk, and the pendulum swings from time to time in opposite directions. To an impartial observer few points clearly stand out in the discussion of the relative value of both suture materials.

Catgut acts as a foreign body and in some individuals is apt to cause around the sutures a tissue reaction in form of an accumulation of serum with fibrin and leucocytic infiltration which, combined with the liquefaction produced in the disintegration and absorptive process of catgut, act as a fertile culture medium for bacteria. Moreover, some authors hold that catgut, a product derived from animal tissues, may be responsible for allergic reactions, although other writers consider the alleged antigenic properties of catgut a myth. Furthermore, there is uncertainty as to the time required for the absorption of catgut. Consensus is that catgut should not be used to suture the skin because suppuration invariably develops. Finally, the cost of catgut is relatively high.

On the other hand, the use of silk also has its limitations. The presence of infected wounds is considered by great many surgeons as a contraindication to the employment of silk, as sinuses may form. This statement is at variance with Meade and Ochsner's contention that the most important use of nonabsorbable sutures is in the grossly contaminated wounds, and with Shambaugh's claim (13, 14) that the presence of silk in suppurating wounds does not delay the healing process. Thompson agrees with Halsted that the presence of fine silk in suppurating wounds does not seriously impede healing. According

to a prevailing opinion, silk should not be used for suturing the mucous membranes of the gall bladder and the urinary bladder because the sutures may act as nidi for calculi. Another disadvantage of silk is that it loses its strength from repeated sterilizations. The use of silk requires a meticulous technique including avoidance of tight sutures, mass ligatures, blunt dissection, etc. The fact that silk has established its reputation in thyroid surgery, repair of severed tendons and nerves, and other operations requiring a refined technique proves the great value of nonabsorbable suture material in surgery.

The value of cotton, linen, soft annealed steel alloy wire, and other nonabsorbable materials, is known but none of them has attained the popularity of silk and catgut. Inasmuch as the two last mentioned leading suture materials offer the aforementioned disadvantages, a search for good substitutes is justified.

Several years ago, while developing a new method for the preparation of so called corrosion specimens for anatomical studies, I was greatly impressed by the plasticity of a synthetic resin vinylite and it occurred to me that a derivative of this product, called vinyon, could be used as a suture material. Vinyon is a copolymer of vinyl chloride and vinyl acetate. The product lends itself to processing which permits manufacture of yarns with a wide range of tensile strengths and elastic properties. An ever increasing use is found for them in various branches of the textile industry. What facilitates the evaluation of vinyon in surgery is the fact that, unlike any other synthetic fiber, the tensile strength of the material is of the same magnitude in both the wet and dry stage. Furthermore, vinyon has a true elasticity comparable with that of silk, a unique property in synthetic fibers. The multifilament yarn is water-resistant, is not



Fig. 1, left. Undyed zytor No. 0 implanted into a sacrospinal muscle of a rabbit. Specimen removed 3 days later. Low power magnification. Few degenerating muscle cells, very few polymorphonuclear leucocytes and a number of young fibroblasts.

Fig. 2. Same specimen, high power magnification. Several polymorphonuclear leucocytes; few muscle fibers degenerating due to the compression by the suture, several macrophages.

attacked by bacilli and fungi, and will not support such growth. Being thermoplastic, the product cannot be autoclaved for purposes of sterilization, but immersion in grain alcohol proved to meet all the requirements of asepsis.

On the present market vinyon is cheaper than silk. A cost comparison with linen is difficult because of the wide variation in sizes; however, in coarse sizes, 150 deniers and up, it is about the same or slightly cheaper than linen.

Another similar product, zytor, already on the market, was also tested as a possible substitute for silk. Vinyon is a polyvinyl resin; zytor, commercially known under the name "nylon," is a polyamide resin. Contrary to vinyon, zytor can be boiled or autoclaved and there is no serious effect of either procedure on the tensile strength of the material. After boiling 30 minutes in water, only 2 to 4 per cent and after autoclaving one-half hour at 15 pounds pressure, only 4 to 6 per cent of the original strength is lost. Braided zytor and braided silk are essentially alike in regard to tensile strengths. Zytor is made in two forms: multifilament and monofilament, and the first is braided.

What are the advantages of zytor over silk? Zytor sutures are less reactive in tissue than silk sutures. As far as the monofilament zytor is concerned, another advantage can be pointed out: here we have a noncapillary strand in which there can be no movement of tissue fluids along the strand and no nidation of bacteria. In the multifilament zytor, similar to braided silk, there are two forces of capillarity: (a) the water uptake of each individual fiber itself—in this respect zytor is superior to silk; (b) capillarity due to the small spaces between twisted or braided fibers; this capillarity is identical in both zytor and silk.

As to the relative value of both types of zytor, the multifilament type has the advantage in that knots hold better and the material is more pliable than the monofilament.

The manufacturer states that the price of the monofilament zytor compares with dermal sutures and the price of the multifilament zytor is approximately the same as that of silk.

Tanburg observed 4 cases of skin irritation in women wearing nylon hose. He suggests that the finish or the dye of the stockings rather than the yarn itself may be the cause

of dermatitis. Allergic reactions attributable to zytor suture material have not been observed by me.

To appraise the value of vinyon and zytor, the first mentioned suture material has been used in St. Elizabeth's Hospital in 30 unselected, consecutive clean cases requiring major surgery. In the following 30 cases vinyon was replaced by zytor. Both groups did not consist of an identical material but on the whole were formed by similar operations such as appendectomy, cholecystectomy, hysterectomy, oophorectomy, repair of postoperative hernias. The entire observation was confined to laparotomies. The synthetic suture materials have been employed for buried sutures of the peritoneum and fascia and also for skin closure. The gauge of both materials was an equivalent of catgut No. 000 and 0. Contrary to the customary advice not to use nonabsorbable material for continuous sutures, this mode was employed for closure of the peritoneum and the skin but the fascia was sutured with interrupted stitches. Vinyon or zytor respectively were also used for invagination of the appendiceal stump, approximation of broad ligaments after hysterectomies, ligation of the cystic duct, etc. In no case was there any evidence of irritation of tissues. At the end of 7 to 10 days, the abdominal wounds were completely healed and there were no signs of an inflammatory reaction. Vinyon or zytor and catgut were never employed together. Great attention was paid to the gentle handling of tissues, perfect hemostasis, clean dissection, avoidance of undue tension, and mass ligatures.

Although clinical impressions are notably unreliable, the theoretical considerations and the limited experience with the new suture materials show that they have sufficient merit to warrant further consideration.

#### SUMMARY

Two new synthetic suture materials, vinyon and zytor, have been studied on 60 unselected and consecutive cases requiring laparotomies. No essential differences could be established

between vinyon and zytor. Both are very pliable, can be easily and repeatedly sterilized, do not fray, do not suffer impairment of their tensile strength in a wet stage, are not attacked by pathogenic micro-organisms, are non-irritating to the tissues, insusceptible to the action of tryptic enzymes, apparently non-allergic, and inexpensive. All these properties justify the prediction that the new suture materials will find acceptance in surgery as substitutes for silk and catgut.

Their main advantage over catgut is that of a nonabsorbable material in general, while the new products are superior to the silk (1) because they can be repeatedly sterilized by autoclaving or immersion in alcohol respectively without any untoward effect on their tensile strength, (2) the knots hold better, and (3) last, but not least, the tissue reaction is less pronounced.

Not enough emphasis can be laid on the necessity of a painstaking technique, with special attention to a meticulous care in gentle handling of tissues, perfect hemostasis and ligation of blood vessels without surrounding structures.

Further investigations are necessary to establish the value of these new suture materials in infected or contaminated wounds.

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## THE LIGAMENTUM FLAVUM: ITS RELATIONSHIP TO LOW BACK PAIN

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THE problem of the varied and multiple causes of low back pain has for many years constituted one of the "great unknowns" of modern medicine, yet year by year a small part of this interesting jig-saw puzzle has been changed from the indefinite to the definite gradually but surely forming a part of a definite design which some day will be complete.

On embarking upon the research embodied in this paper we were of the opinion that if one small segment of discussion could be clarified a definite contribution would have been made. This was stimulated by the often repeated, but so rarely answered, simple interrogation "What constitutes the normal ligamentum flavum?" To the uninitiated this seems rather a far flung cry as a contribution to the etiology of a type of low back pain. However, the vast amount of proved cases of sciatic pain with demonstrable intraspinal pathology giving rise to pressure symptoms resulting either from changes of the ligamentum flavum, posterior protrusion of the intervertebral disc or both, has demonstrated the importance of the ligamentum flavum in the low back syndrome.

The structure was first noted to have pathological possibilities by Elsberg in 1913. It was not, however, until Towne and Reichert in 1931, showed that the ligamentum flavum might cause pressure upon nerve roots that its surgical significance was established. These authors attributed the condition to hypertrophy of the normal ligament, and this explanation was accepted by other investigators until recently. Attention was directed solely to size and relationship to the adjacent nerve roots as an explanation of its importance, and increase in size was assumed to be a simple hypertrophy of a normal structure. The ques-

tion that crossed the minds of many has been: "Just what is the average normal and when may the ligament be said to be hypertrophied?"

It was this apparently simple question that caused Spurling and Rogers (11) first to attempt to establish by actual measurement what the "normal" size might be.

The ligament was also studied, measured, and described in comprehensive reports by Abbott in 1936 and 1938 (1, 2), Brown in 1937 and 1938 (3, 4), Naffziger and co-workers in 1938, and Horwitz in 1939.

Our objection to all this painstaking antecedent work is that the material was obtained from fixed cadavers and therefore did not establish a base line to which the normal and the abnormal could be compared, macroscopically and microscopically under *analogous conditions* to those found in the *living patient*.

The primary endeavor in our work therefore was to obtain fresh surgical specimens, to measure them under a standard technique, and to study them microscopically with standard methods of fixation and staining. This research was started in 1939, and while still in progress, Dockerty and Love from the Mayo Clinic in March, 1940, reported their results of measurements and microscopic findings in a series of 50 ligaments removed at operation for sciatica and backache.

Although, as we shall attempt to show, we do not attach much significance to the measurements given, our findings and conclusions from a histopathological standpoint strike a close parallelism.

As a result of this search for the "simple normal" it has been proved to our satisfaction that the so called "hypertrophy" of the ligamentum flavum does not represent an increase in size of the normal tissue, but rather a definite pathological change in the constituent elements of the tissue with a "substitution fibrosis" of varying degrees and amounts re-

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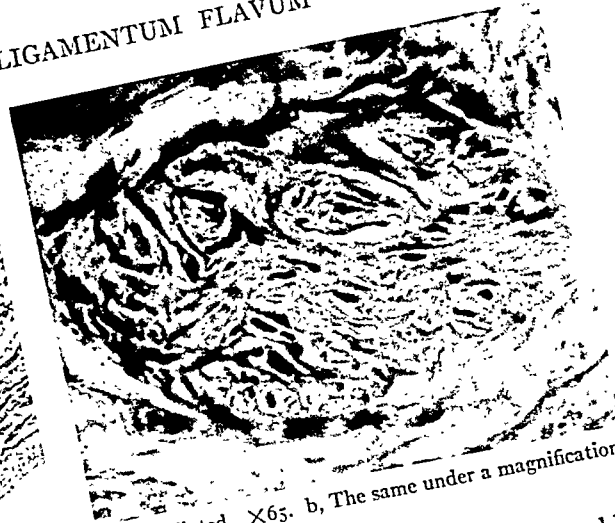


Fig. 1, a, left. Photomicrograph showing a nerve trunk or ending within a ligamentum flavum. The fibers are chiefly nonmedullated.  $\times 65$ . b, The same under a magnification of 325 diameters.

placing the normal yellow elastic fibers, thus accounting for its change in size and appearance. We noted further that these pathological changes were not confined alone to that group of ligaments causing pressure phenomena and that similar pathology was apparent in specimens of ligamentum flavum removed for causes other than those producing intraspinal defects and nerve root pressure.

We soon found ourselves deviating from the realm of the concrete to the speculative as we attempted to correlate the clinical relief obtained in cases of kissing spine, localized trigger point pain in the lumbar region for which we had removed the ligamentum flavum and found the same histopathological changes.

The recent work of Steindler and Luck (12, 13) seemed to offer a logical explanation, if the pathological changes in the ligament were to be attributed as the etiological factor for this "posterior syndrome."

According to these authors, the nerve sinuvertebralis, which receives a white ramus from the common trunk and a gray ramus from the sympathetic chain just outside the intervertebral foramina and then turns back into the intervertebral canal supplying the neck and head of the rib, the pedicles, interior of the bodies of the vertebra, the loose areolar perimeningeal tissue and periosteum, was described about 1850, by Purkinje and von Luschka. They believe that reflex pain may be referable, on this basis, to lesions in and

about the intervertebral canal and were able to break the reflex arc by injection of the localized "trigger points" with novocain.

In the type of case under discussion we, likewise, were able temporarily to alleviate the pain by a similar technique. No reference was made, however, to the innervation of the ligamentum flavum, and the question of its nerve supply, if any, demanded further investigation.

Reference to the literature revealed Spurling and Bradford (10) quoting some recent unpublished studies by Roofe, who found a profuse supply of sensory nerve endings in the annulus fibrosus and posterior longitudinal ligaments.

In this connection by special selective staining methods we have been able to demonstrate the presence of non-medullated nerve fibers in the ligamentum flavum, as illustrated in Figure 1. These findings substantiate the work of the previously mentioned investigators and specifically demonstrate a nerve supply to the yellow ligament. It might offer a logical explanation for the referred pain found in these cases and the reason for its alleviation by surgery.

## BASIS OF PRESENT REPORT

We are reviewing 26 cases in which ligamenta flava were removed at operation, measured, and studied microscopically. These specimens were taken regardless of whether they





Fig. 2 Dissected specimen of ligamentum flavum from the level 4 to 5 lumbar a, View from laterally, b, view from caudal margin, c, view as from within spinal canal

were suspected of causing backache and whether they were related to a herniated intervertebral disc.

As a basis for microscopic comparison, cadaver specimens at various age groups, without known history of back trauma, were used.

Specimens studied were removed from cases of "congenital low back", vertebral disease, "kissing spine," "trigger-point" pain in post-traumatic low back disability without intra-spinal protrusion. Microscopic sections were studied by differential staining methods, including hematoxylin and eosin, Mallory's connective tissue stain, Weigert's and van Gieson's. More than 400 sections were examined. It was found that selective stains for elastic fibers, especially the van Gieson, gave the most information

#### FALLACIES OF MEASUREMENT

A brief survey of the anatomy of the ligamentum flavum will demonstrate the ease with which errors of measurement can be made. This structure is a saddle shaped mass of connective tissue, light yellow in color and tough in consistency. It bridges the space between the laminae, extending laterally to blend with the capsules of the lateral articulations, assuming its greatest thickness dorsally, mesially, and thinning out laterally in both directions.

It is apparent that, in order to obtain any standard of comparison, measurements must be made in analogous locations, as variations in thickness may be as high as a hundred per cent in the same specimen. Due to the elasticity of the structure, the degree of tension placed on the ligament is equally important. Our measurements were carried out with a micrometer with a constant bearing area and tension at a specified selected site. Fragments

were discarded in which the planes could not be accurately orientated. It was found that specimens varied to such a degree with the size and development of the individual that no accurate generalization could be made as to the responsibility for symptoms from this factor. Moreover, of our two thickest specimens, both found in conjunction with herniation of a portion of the intervertebral cartilage in heavy, well developed young individuals, one specimen was normal histologically, according to our criteria, and one abnormal.

It is our conclusion, relative to macroscopic appearance, that the "normal" varies with the age, weight, physical development of the individual and the anatomical location of the ligament. Postural curves and spinal architectural deviations from the normal, with the presence of congenital anomalies, contribute to the variation.

It is not the size of the ligament alone, but the interrelationship of these factors, with or without pathological changes in the ligament that determines whether, in any particular case, the ligament is a causative factor for symptoms.

A typical example of the interrelationship of these factors (L. M., case 22 in series) was recently seen by one of us (M. C. M.). This patient had a moderate flexion injury to his lumbar spine one year previously followed by recurrent low lumbar backache with radiation of pain down one or both legs on effort. Although the pain was of sciatic type there were no sensory changes and no asymmetry of his reflexes. There was demonstrable roentgenologically a congenital anomaly of the articular facets of the third lumbar vertebra allowing the inferior articulations on both sides to be deviated toward the midline due to rotary changes in the isthmus.

Temporary relief only could be obtained by leg traction and a flexion plaster. Spinal puncture demonstrated a complete block below the level of the second lumbar and this was confirmed by air and lipiodol myelography.

At laminectomy a complete block was found due to the combination of the bony anomaly, a complete rupture of the third lumbar intervertebral disc, and the ligamentum flavum. It is certain that any of these factors taken sep-

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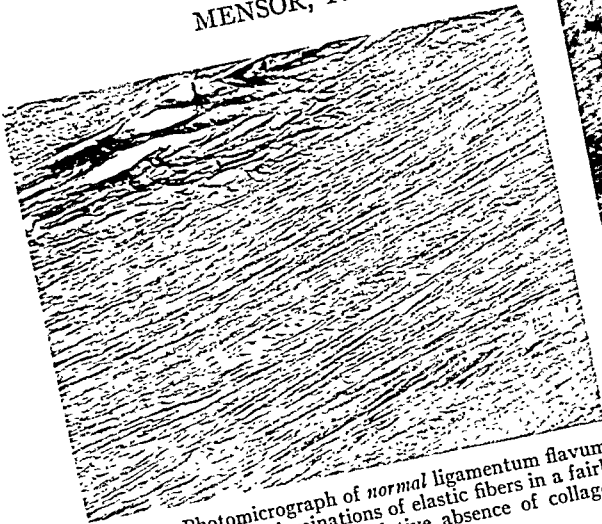


Fig. 3. Photomicrograph of *normal* ligamentum flavum.  $\times 65$ . Note parallel laminations of elastic fibers in a fairly uniform wavy pattern, and relative absence of collagen elements.

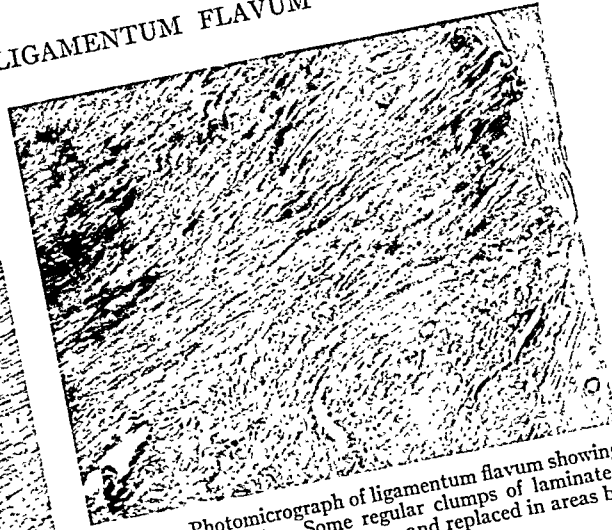


Fig. 4. Photomicrograph of ligamentum flavum showing *slight* fibrosis.  $\times 65$ . Some regular clumps of laminated fibers still evident, but broken up and replaced in areas by collagen elements.

arately would not have given such a picture. This case is likewise unusual in having a rupture of the fourth intervertebral disc as well, all in the absence of obvious neurological findings.

## HISTOPATHOLOGICAL FINDINGS

Histologically the ligamentum flavum is mesenchymal in origin, composed of specialized connective tissue. The three basic fibers of the connective tissue stroma are collagen, elastic and reticular fibers. The elastic fibers

originate from a substance known as elastin, and give to the ligament its characteristic yellow color.

The normal ligamentum flavum consists of regular laminated bands of elastic fibers constituting an estimated three-fourths of the ligament. Collagen and ordinary adult connective tissue cells can be seen to make up about 30 to 50 per cent of the tissue volume. This is not seen, of course, in specimens stained selectively for elastic tissue; in fact, as one looks at such a preparation there would

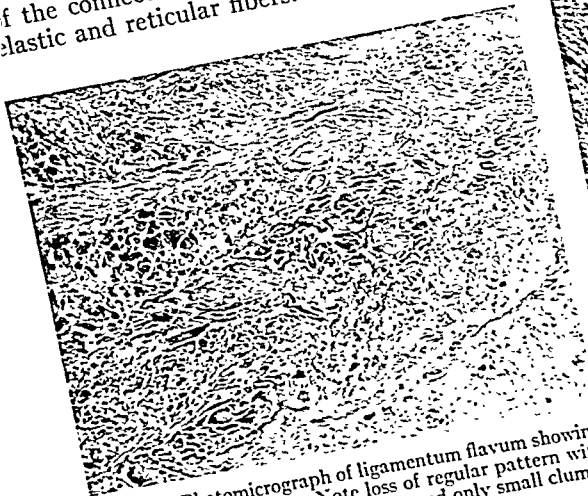


Fig. 5. Photomicrograph of ligamentum flavum showing *moderate* fibrosis.  $\times 65$ . Note loss of regular pattern with predominance of collagen elements, and only small clumps of elastic fibers.

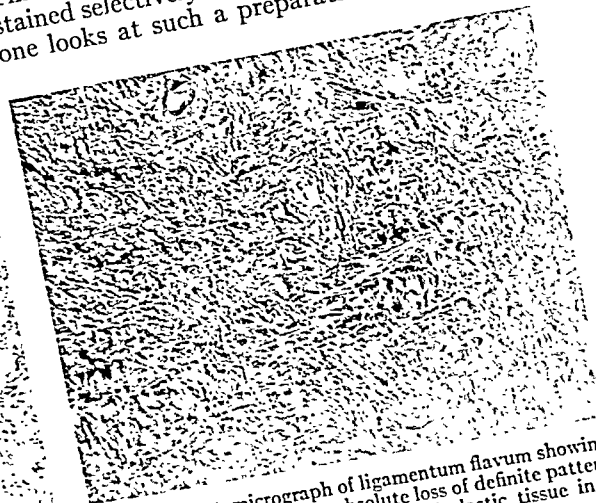


Fig. 6. Photomicrograph of ligamentum flavum showing *severe* fibrosis.  $\times 65$ . Note absolute loss of definite pattern with only small, isolated elements of elastic tissue in a matrix of collagen substitution fibers.

seem to be little room for other tissue. When contiguous selections are otherwise stained, however, the relative importance of other connective tissue elements is apparent. Nor are the fibrocytes uniformly distributed through the sectioned ligament. They tend to be most prominent at the periphery (in all planes).

The yellow elastic fibers stream through the sections in broad, interlacing bands, interspersed in a definite wavy arrangement by collagen fibers through which an occasional blood vessel is seen. Fibrocytes are uncommon except at the margins of the ligament.

Toward the periphery of the normal ligament the orderly arrangement of the laminations is disrupted. The design is less compact, fibrocytes are more numerous, especially near the osseous attachment, some fatty tissue is present, and blood vessels are more in evidence. These blood vessels are thick walled.

The decision as to what is "normal" and what is "abnormal" among our specimens has been difficult. We have noted a variation in grade of abnormality from what we term a very slight fibrosis to marked fibrosis.

These abnormal findings are characterized by a progressive loss of the regular pattern with a break-up of the laminations of the elastic fibers and replacement in varying degrees by collagen fibers. The elastic fibers are sometimes fibrillated, broken in small clumps, or replaced by the collagen element. Gradations of change have occurred from slight disruption of the normal architecture to almost complete substitution by collagen.

#### ANALYSIS OF RELATIONSHIP OF PATHOLOGICAL LIGAMENT TO BACK PAIN

In cases with sciatica and evidence of nerve root irritation we have found no constant relationship between histopathological changes in the ligament and the symptom complex. Both in cases of proved dislocation of the intervertebral disc and those in which the ligament was felt to be the responsible factor, the microscopic findings have varied from normal to moderately advanced fibrosis. Indeed, in at least one case in which a normal ligament, microscopically, had been removed, there resulted a complete alleviation of symp-

toms. This leads us to reiterate, it is not necessarily the size or pathological changes in the ligament, but rather its relationship in the particular individual, that betokens its clinical importance in this type of case.

#### LIGAMENTS REMOVED FOR CAUSES OTHER THAN SCIATICA

In this series we found some of our most extensive fibrosis. In those cases in which a spinal fusion was performed, unfortunately, we shall be unable to determine what significance the demonstrable change in the ligamentum flavum might have had. However, the 3 cases in which the ligament was removed together with the interspinous ligament for "trigger point" pain, have resulted in complete alleviation of symptoms. We have previously speculated as to the relationship of these pathological changes in the yellow ligament to localized chronic back pain following trauma. As opportunities present themselves, we expect to make further observations upon this matter.

It seems prudent to call to the attention of other investigators that we believe that degenerative factors of age and use enter into the pathological picture of this structure as it does in other tissues. To illustrate this point, one of our series was a man of 65 years. In this case, sections showed replacement of the elastic fibers by collagen elements to the extent of about 90 per cent. In this patient surgery instituted for a demonstrable intraspinal block was not followed by relief of pain in the back.

#### CONCLUSIONS

1. Size and thickness of the ligamentum flavum alone are unimportant as possible etiological factors in back pain and sciatica, unless changed by trauma or disease, or causing pressure symptoms in combination with skeletal and/or nuclear changes.

2. Measurements are unreliable due to technical factors which prevent the establishment of any fixed standards. Size and thickness varies with age, anatomical and pathological structural changes, and location in the individual case.

3. The ligamentum flavum reacts to disease or trauma by the loss of the normal archi-

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ture of the elastic fibers and the development of a "substitution fibrosis" with replacement by collagen elements in varying degrees.

4. Definite degenerative factors occur in this structure with advancing age, giving similar pathological changes to those seen in trauma and disease.

5. The term "hypertrophy" is unsuitable as no increase in elastic elements with the preservation of the normal histological appearance has been observed.

6. A definite nerve supply—chiefly nonmedullated in type—to the ligamentum flavum has been demonstrated and presents a further anatomical explanation for certain aspects of "Steindler's posterior syndrome."

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## THE MECHANISM OF URETERAL OBSTRUCTION IN PROLAPSE OF THE UTERUS

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**I**N 1847 Virchow was the first to call attention to the fact that complete prolapse of the uterus was frequently accompanied by hydroureter and hydronephrosis. Subsequently, Froerich, quoted by Brettauer and Rubin, reported a case of prolapse of the uterus with fingerwide dilatation of the ureters. He believed that the ureteral dilatation was due to a stasis in the bladder caused by a kinking of the urethra.

In 1907, Halban and Tandler carried out careful topographic studies on 23 cadavers with prolapse of the uterus. In 15 of these the ureters were dilated. They called attention to the fact that the entire ureter was dilated except the distal portion near the bladder. The dividing line between the dilated and undilated portion of the ureter corresponded with the edge of the levator muscle which forms the lateral border of the hiatus genitalis, or genital rupture ring through which the prolapse of the uterus and of the urinary bladder occurs. As a result of the descent of these organs through this ring, the ureter is pressed against the edge of the levator muscle and occluded by compression.

Brettauer and Rubin in 1923, following a careful review of the literature, felt that the mechanism of ureteral occlusion in prolapse of the uterus might be explained in one of the following ways: (1) kinking of the urethra and stasis in the cystocele (hourglass formation of the bladder), (2) intramural stretching in the bladder wall with stenosis; (3) compression of the ureters outside of the bladder. They also mentioned that the uterine artery might play a rôle in compressing the ureter.

Schmitz and Laibe in 1929 studied the changes in the upper urinary tract in prolapse of the uterus. They came to the conclusion

that the hydroureter and hydronephrosis in procidentia are caused by a combined torsion, kinking, and edema of the ureter in its vesical portion.

Wallingford in 1939 suggested that the uterine artery in prolapse formed a sling over the ureter and produced a compression of the latter when the uterus descended.

Maher and Wosika in 1939 reported that prolapse of the uterus is frequently accompanied by a hypertension. In 97 cases of procidentia studied by them, hypertension occurred in 74, or 76 per cent. They ascribed the hypertension to hydronephrotic changes in the kidneys and stated that "while the exact mechanism of ureteral compression does not seem entirely clear, obstruction is consistent with complete prolapse." In fact these authors in making their intravenous urograms used the compression effect of pulling the prolapsed uterus downward instead of the conventional abdominal compression.

From these studies it is clear that although numerous theories have been advanced as to the manner in which the ureters may become occluded in procidentia, proof of the exact mechanism has not heretofore been given. It is, therefore, the purpose of this paper to present a new mechanism and to demonstrate it upon the living subject by roentgenographic means.

In order to appreciate the manner in which the ureter may become occluded it is necessary to review the fundamental topography of the ureter in the female pelvis. From its origin at the ureteropelvic juncture the abdominal ureter courses downward in back of the posterior parietal peritoneum, to which it is more or less loosely attached. As it dips down into the pelvis over the linea innominata, it crosses the external iliac vessels. It then courses downward, forward, and medially through the broad ligament, lateral to and at a varying distance

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Fig. 1. Second degree prolapse of the uterus. Roentgenogram with ureter catheters in place and the uterus pulled downward. The left ureter shows an acute downward angulation.

from the cervix uteri. After a short interval it enters the wall of the urinary bladder.

The course of the abdominal ureter is best observed through the routine lumbar kidney incision. As the parietal peritoneum is stripped forward from the posterior abdominal wall, the ureter, which is loosely attached to the peritoneum, moves forward with it.

The pelvic ureter, however, is best approached through a laparotomy for the purpose of topographic study. As it crosses over the external iliac vessels in descending into the pelvis, it is covered only by the pelvic peritoneum. It is freely movable at this point and is easily located by palpating the pulsation in the iliac artery. If the overlying peritoneum is then incised, thus exposing the artery for a short distance, the ureter will be seen crossing it. The ureter may then be lifted out of its bed and dissected free in a downward direction, with ease, until the broad ligament, in which the ureter lies firmly imbedded, is reached. During its course through the broad ligament the uterine artery crosses above the ureter—occasionally it may cross below it.

It, therefore, becomes evident that the ureter has three fixed points of attachment: (1) at its origin from the renal pelvis, (2) during its course through the broad ligament, and (3) at



Fig. 2. Third degree prolapse of the uterus. Roentgenogram with ureter catheters in place and the uterus pulled downward. There is a deep downward angulation of the left catheter which has also been pulled down out of the upper ureter.

its entrance into the wall of the urinary bladder. Elsewhere it is more or less freely movable. Whereas a huge retroperitoneal or renal tumor may dislocate the upper ureter even beyond the midline without causing an appreciable ureteral compression, a tubo-ovarian abscess which points into the broad ligament or an intraligamentary fibroid may cause serious ureteral obstruction.

The broad ligament, in which the ureter lies so firmly imbedded, also plays an important rôle in supporting the uterus under normal conditions. Mengert in 1936 carried out a very careful study on the cadaver to determine the exact structures which support the uterus, and how impairment of these structures leads to procidentia. He placed each cadaver on its back on a table in a horizontal position. With the aid of tenaculum, a cord was attached to the cervix and carried over a pulley at the foot of the table, where a 1 kilogram weight was



Fig. 3. Third degree prolapse of the uterus. Roentgenogram with ureter catheters in place and the uterus pulled downward. There is a deep downward angulation of the left ureter. The apex of the kink descends down through the pelvic outlet.

fastened to the cord. In this manner a horizontal pull of 1 kilogram was exerted on the cervix. He then opened the abdomen and divided various structures adjacent to the uterus. When the infundibulopelvic ligaments, the

round ligaments, and the upper third of the broad ligaments were divided, no descent of the uterus occurred. But when he divided the lower two thirds of the broad ligaments, considerable descent followed. When the paravaginal tissues on both sides were divided, complete prolapse was accomplished. The supporting structures according to Mengert are fibrous tissues which extend laterally in a broad band from the lateral aspect of the cervix and lower portion of the corpus, to attach to the fascias at the pelvic brim. A similar band of fibrous tissue likewise extends laterally from either side of the vagina to the brim of the pelvis. The fibrous tissues in the lower part of the broad ligament have also been described as a dense band which is known as Mackenrodt's ligament.

In summarizing these findings it is seen that a dense band of fibrous tissue lies in the lower two thirds of the broad ligament between its peritoneal coverings. This band extends laterally from the cervix and lower portion of the corpus to the pelvic brim. The ureter in its course through the broad ligament lies firmly imbedded in this portion of the broad ligament.



Fig. 4. Third degree prolapse of uterus. Roentgenogram with ureter catheters in place, uterus pulled downward. Note acute shallow, downward angulation of both ureters.



Fig. 5. Third degree prolapse of the uterus. Roentgenogram with ureter catheters in place and the uterus pulled downward. There is a deep, sweeping, downward looping of both ureters which have descended out of the pelvis. The catheters have been pulled down out of the upper ureters by this descent.

It is, therefore, our opinion that when prolapse of the uterus occurs, the broad ligament, with its contained fibrous tissues, forms a sling which pulls the ureter downward and produces a kinking as well as a compression of the latter. If this is the case, this mechanism should be readily demonstrable in procidentia on the living subject by roentgenographic means.

Ten patients with prolapse of the uterus were selected for this study. Roentgenographic studies of the ureters were carried out with the uterus in the normal position and after it had been pulled down with a tenaculum attached to the cervix. At first an attempt was made to demonstrate the lower ureter by intravenous urography and then by retrograde pyeloureterography; but both of these methods proved unsatisfactory because the lower ureter failed to show when the uterus was pulled downward, probably because the dye was driven away from this region by the kinking and stretching of the ureters.<sup>1</sup>

It was, therefore, decided to delineate the course of the ureters by inserting thin, soft, radio-opaque catheters to the renal pelves and to take roentgenograms with the uterus in the normal position, and after it had been pulled downward. At first anteroposterior, lateral, and oblique views were taken. But since it soon became evident that the anteroposterior exposure best showed the changes in the course of the ureter, and since the additional views did not give any further information, we decided to confine ourselves to the former.

As was to be expected, when the uterus was pulled downward, the changes in the ureters varied from a short, acute, downward kink to a wide, sweeping downward curve, which carried the ureter down out of the pelvic outlet. In fact, in one case this downward sweep was so pronounced that the tips of the catheters were pulled down in the ureters for a considerable distance. These changes were most pronounced in the cases of complete prolapse, and they were either unilateral or bilateral. Occasionally they were absent. Such an absence of the kinking of the ureter on one or both sides may be explained in the following manner:

The very disintegration and relaxation of the fibrous bands in the broad ligament which contribute to prolapse of the uterus may have progressed to such an extent that these structures are no longer sufficiently intact to form a sling over the ureter when the uterus descends. More specifically the findings when the uterus was pulled down in the 10 cases studied were:

In 3 cases of first degree prolapse: 2 cases showed no alteration in the course of the ureter; in 1 there was a short, acute, downward angulation of the left ureter.

In 3 cases of second degree prolapse: there was no alteration in the course of the ureters in 1 case; the lower ureters descended (by stretching) but no angulation was seen in 1 case; there was a slight downward angulation of the left ureter in 1 case (Fig. 1).

In 4 cases of the third degree prolapse: there was an acute deep downward angulation of the left ureter in 2 cases, which was so deep in 1 instance that the apex of the kink descended out of the pelvis (Figs. 2 and 3); in 1 case there was a shallow, sharp, downward angulation of both ureters (Fig. 4); in 1 case there was a deep, sweeping downward looping of both ureters which descended well out of the pelvis. As a result, the ureter catheters were pulled down out of the upper ureters (Fig. 5).

#### SUMMARY

1. It has long been known that complete prolapse of the uterus is frequently accompanied by ureteral obstruction, which may lead to a dilatation of the ureters and renal pelves.

2. Although numerous theories have been offered as to the manner in which this obstruction is produced, the exact mechanism has not previously been demonstrated.

3. On the basis of topographic anatomical studies, a new mechanism is suggested. The broad ligament with its contained fibrous bands, which are attached laterally to the fascias at the pelvic brim and medially to the cervix and corpus uteri, forms a sling over the ureter and pulls it downward when the uterus descends. This produces a marked downward kinking of the ureter.

4. This downward kinking of the ureter is readily demonstrable on the living subject by radiographic means.

<sup>1</sup>This undoubtedly explains why the exact mechanism of ureteral obstruction in uterine prolapse has not been demonstrated previously in any of hundreds of roentgenographic studies which have undoubtedly been made in such cases in the past.



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## INTUSSUSCEPTION IN ADULTS

## A Consideration of Therapeutic Measures and a Case Report

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**I**NTUSSUSCEPTION is preponderantly an affliction of infancy and early childhood with 75 per cent of the cases occurring in individuals under 2 years of age (21, 30); the disorder is relatively uncommon among adults but it is always critical and may afflict an individual of any age.

The intussusception of infancy is usually idiopathic, and while in adults it may likewise be idiopathic it usually, about 70 per cent of the cases (30), is associated with the presence of a tumor, a diverticulum, or an ulcer. In a group of 300 adult cases of intussusception analyzed by Eliot and Corscaden, one-third was due to tumors of which 60 per cent were benign. Martin and Love report intussusception following trauma and state that 4 other such cases have been recorded. A number of cases involving the sites of gastric and intestinal anastomoses have also been reported (7, 10), as have several instances of primary intussusception of the appendix (29).

Christopher stated in 1936 that, since Eliot and Corscaden's paper of 1911, 43 cases of adult intussusception due to benign tumors and 16 cases due to malignant tumors had been reported. These consist of the following varieties: of the benign group there were lipoma, 11 cases, adenoma, 9 cases, fibroma, 9 cases; polypi, 5 cases, papilloma, 2 cases, myxoma, 2 cases, leiomyoma, 1 case, carcinoid tumor, 1 case, enterocystoma, 1 case, adenoma of accessory pancreases, 2 cases of the malig-

nant group there were carcinoma, 10 cases; and sarcoma, 6 cases.

Christopher also stated that "twenty-five cases of intussusception in adults have been reported in which no tumor was found or at least described." He added one more case to this group and also one case to the tumor group. In the 3 years since his paper somewhat over two hundred reports concerning adult intussusception have been published in the world literature. Excluding those associated with concurrent abnormalities, only 14 idiopathic adult cases have been presented in the English literature during this period (4, 5, 6, 11, 15, 25, 32, 33). In this group 3 were proved by examination after resection and 1 was proved by postmortem examination; all the others were carefully inspected and palpated for evidence of causative pathology and none was found. The present paper describes an additional case belonging to the idiopathic group. This case occurred in the author's practice, and an account of it is presented in the appended report.

Intussusception of the gastrointestinal tract may occur at any point between the stomach and the rectum. Inasmuch as tumors are more common in the large bowel it is not surprising to find that the latter is more often the site of involvement in adults than is any other portion of the gastrointestinal tract.

The direction of the intussusception is nearly always descending. Lockhart-Mum-

mery states that, "retrograde intussusceptions do occur but only during death or as a result of asphyxia; they are not met in practice." Rosenblum writes, "ascending or retrograde intussusception occurs, probably, only just before death or at the time of death." Nevertheless, several such cases occurring during life have been reported in the last four years (9, 12, 15, 19). Moreover, a number of retrograde intussusceptions involving anastomoses have been recorded (7).

#### TREATMENT

Intussusception is a form of strangulation obstruction, the therapeutic approach to which involves the following considerations: (a) reduction, thereby relieving the obstruction and the circulatory impairment; (b) evaluation and disposition of the involved segment of bowel; (c) correction of possible etiological factors.

In common with other forms of strangulation obstruction, early diagnosis and treatment are prerequisites to successful treatment, though it is agreed that subacute and chronic cases may occur, and that, occasionally, a case may recover spontaneously by self-reduction or by sloughing the gangrenous segment and establishing an autoanastomosis. In contrast to other forms of bowel strangulation it is to be noted that this form may occur without localized tenderness or muscle spasm owing to the fact that the strangulated segment, the intussusceptum, is ensheathed by the intussusciens which thereby protects the parietal peritoneum from irritation. Appreciation of this fact is of importance and especially so in the early diagnosis of the disease.

*Reduction.* Two methods of reduction may be considered: (1) indirect manipulation by administration of enemas, and (2) manipulation through an abdominal incision. The former method is applicable only in instances of colocolic and ileocecal intussusception as it consists in an attempt to force back the intussusceptum by building up a head of pressure against it through the administration of air or fluid enemas. Besides being limited in application this type of treatment is redundant with potential dangers and is more appropriately applied in the treatment of the condi-

tion in infants and children. Indeed, the really enthusiastic proponents of this form of treatment seem to have attained their success in the infancy and childhood age groups. Hipsley, whose report is notable, has demonstrated that it is a meritorious therapeutic measure in skilled hands. He states that he has successfully reduced 65 of 100 consecutive cases with a mortality of only 5 per cent for the entire group. Admirable as these results are, it should be realized that not many surgeons have had extensive experience in treating such cases, and consequently are not in a position to acquire the proficiency of judgment which will permit them to recognize readily the cases of incomplete reduction. Furthermore, in infants and children the intussusception is usually uncomplicated by other pathological conditions, whereas in adults the reverse is true and operative procedures are commonly necessary to eradicate the causative pathological process. Obviously, hydrostatic treatment does not permit the removal of a tumor or a diverticulum nor does it permit recognition of nonviable bowel. Injudiciously applied hydrostatic pressure may cause perforation of the bowel if exerted against a devitalized bowel wall, and especially so in one involved by tumor.

Retrograde intussusceptions, though rare, do occur and usually are not recognized preoperatively. In these instances the administration of enemas would certainly be contraindicated. Moreover, a seriously sick patient who may ultimately have to come to operation would not be improved as a surgical risk if treated previously by colonic distention.

The use of barium enemas under fluoroscopic control as a diagnostic aid, on the other hand, is often indicated for it enables one to ascertain the position of the lesion and it may even identify the intussusception. An abdominal roentgen film without the administration of contrast media, can and should be taken in all suspected cases, for, as recently pointed out by Schatzki, the roentgenological diagnosis of intussusception can often be made on the basis of this alone.

*Manipulation through an abdominal incision.* The first maneuver which is usually employed in manual reduction is the application of

manual pressure over the apex of the intussusceptum with coincident light traction on the proximal free bowel. It is essential that such a procedure should be executed with gentleness for overzealous efforts may result in tearing the bowel or mesentery which, because of edema and impairment of circulation, is abnormally susceptible to the trauma of traction. Frequently an appreciable degree of edema is present in the proximal portion of the intussusception and may cause sufficient constriction to make withdrawal of the intussusceptum difficult or impossible. One may attempt to overcome such a condition by compressing the mass at the point of constriction, thereby squeezing out some of the edema fluid into the adjacent tissues. Sometimes it is possible to insert a finger gradually between the intussusciens and intussusceptum and dilate the neck of the passage; in addition, a finger tip so introduced may be hooked into the wall of the intussusceptum, thus permitting light traction distal to the constricted point. In the case reported in this paper the intussusceptum was spirally twisted and reduction was accomplished only after a finger had been inserted as above described and manipulated in a manner partially to unwind the spiral formation; approximately 2 inches could be unwound at once and this portion was then easily withdrawn, following which further unwinding and withdrawal was possible. By these alternate manipulations reduction of about 12 inches of bowel was accomplished and then the remainder of the invaginated loop was easily withdrawn.

*Management of irreducible intussusception.* Occasionally the neck of the invagination is so tight that the above manipulations are ineffective and under these conditions it may be incised with scissors just as one performs a dorsal slit for phimosis. This procedure is advocated by Brown. It will frequently release the incarcerated segment which may then be drawn out. The incision is best made on the antimesenteric side of the bowel, and following reduction the incision is closed by a double row of sutures.

The Jesset operation has also been advised for the treatment of irreducible intussusception (28). This operation consists of incising

the intussusciens and from within its lumen amputating the intussusceptum as high as possible. An operation of this character may permit the correction of the deformity but exposes the patient to the danger of peritonitis as it requires a large incision in the bowel wall and involves a considerable amount of manipulation by instruments and hands in contact with intestinal mucosa. Contamination of the peritoneum under such conditions is almost unavoidable. Consequently, the operation must be regarded as likely to be unsatisfactory and fraught with danger.

A very satisfactory procedure to which one may resort is fixation of the intussusception *in situ* with interrupted sutures about its neck and sidetracking it by means of a lateral anastomosis, the success of which depends upon the relief of the obstruction, and also upon the protection of the peritoneum by the viable wall of the intussusciens. Frequently the intussusceptum sloughs off and is passed spontaneously through the rectum. The following reports exemplify the rationale of such treatment.

Kingsford reported the case of a 46 year old man in which, owing to the critical condition of the patient, he limited the operative procedure to a lateral anastomosis between the ileum and transverse colon. Six days later 18 inches of necrotic bowel was passed by rectum. The patient recovered. Montgomery and Mussil reported 2 similar cases in infants. Recovery followed, though no slough was passed.

Bockoven, Thompson, and Mayo have each reported cases in which the diagnosis was missed, no operation was performed, and spontaneous recovery was accompanied by the passage of the sloughed bowel segment.

Pryde reported the spontaneous passage of 6 inches of intussuscepted small bowel in a post partum patient who was discharged apparently well 14 days later. However, 2 weeks later the patient was operated on because of a recurrence of symptoms. An obstruction due to inflammatory reaction at the site of the auto-anastomosis was found. Resection and end-to-end anastomosis was then done, and the patient recovered. This case is illustrative of the wisdom of the advice of Eliot and Corscaden

These authors reviewed 43 cases in which the necrotic bowel passed spontaneously per rectum; in some of the cases lateral anastomosis alone had been performed and in the remainder no operation had been done. They concluded that, "in cases cured by sloughing although temporary relief is usually afforded by nature's method, yet within 18 months, and usually much earlier, secondary obstruction develops from cicatricial contraction at the point of the original invagination, and is rapidly fatal. Such an unfortunate termination appears so common that after the subsidence of the abdominal symptoms associated with the discharge of the slough in these neglected cases, the writer suggests the advisability of providing against the contingency of subsequent obstruction by establishing a lateral anastomosis between the intestinal canal on either side of the invagination."

This opinion is well substantiated by the experimental work of Montgomery and Musil, who created artificial intussusception in 25 dogs. In 11 of the dogs they also created a short circuiting anastomosis. The 11 dogs with the anastomoses lived and remained well, but when killed and examined 60 days later they all presented cicatricial contractures at the site of the sloughed invagination. Of the 14 dogs without anastomoses 2 died from hemorrhage 2 days after operation, 2 died from acute obstruction within 5 days, 1 showed no evidence of obstruction either antemortem or postmortem, and 9 dogs lived an average of 34 days before dying of chronic bowel obstruction.

From this evidence it may be deduced that an irreducible intussusception can be safely left within the abdomen provided the immediate obstruction is relieved and the eventual cicatricial stenosis at the site of the sloughed invagination is provided for. This may be done by a short circuiting anastomosis or, in certain poor risk cases, by a colostomy or ileostomy as a first stage procedure with subsequent short circuiting or resection of the stenosed area of colon. Such a solution to a difficult problem has a great deal of appeal, for it is an acceptable method whereby the surgeon may shunt an acutely ill patient around the dangers of a resection. It is espe-

cially valuable when dealing with infants and children in whom resection is so often fatal.

*Management of prolapsed sigmoidal intussusception.* The fact that some sigmoidal intussusceptions prolapse through the anus renders them unique and makes possible a special operative approach to the problem of disposal of the affected bowel. The method to be used is similar to that employed in the rubber band treatment of rectal prolapse as advocated by Reid. Wangenstein (31) and Bayard each reported a case successfully treated by the application of a rubber band in such a manner that the prolapsed sigmoidal intussusception sloughed off at its neck.

The technique used in these cases in general was as follows: Under spinal anesthesia with the patient in a steep Trendelenburg position, a firm rubber tube approximately 1 inch in diameter was passed through the lumen of the invaginated and prolapsed sigmoid to a level several inches beyond the point of involvement; a tight rubber band was then slipped up over the invaginated sigmoid to the level of origin of the invagination. The intussuscepted sigmoid eventually sloughed off due to the constriction of the bowel wall between the rubber band and rubber tube and an auto-anastomosis was established. In Bayard's case the band was placed about 5 inches above the level of the anus, and the slough came away on the ninth day. Wangenstein reported separation of the slough on the fifteenth day and noted that it occurred at a point about 1 inch above the level of the constriction. Bayard's case was symptom-free 1 year later and at that time showed no evidence of stricture of the rectum. If stricture should develop following this type of operation, it would be fortunately at a point amenable to dilatation. It has been suggested by Wangenstein that gas gangrene antitoxin be given prophylactically in such cases.

The above procedure appears to offer a rather simple method whereby intra-abdominal resection may be avoided in patients with sigmoidal intussusception with prolapse, which are irreducible or nonviable, or both. It is essential that the surgeon be able to reach the neck of the invagination and he must be certain that no loops of small bowel have become

insinuated between its walls if the manipulation described is to be carried out with complete safety. Laparotomy might well complement this operation, for by it, one could better evaluate the magnitude of the lesion, locate more accurately the point for constriction, and be assured that no loops of small bowel are involved in the process.

**Resection.** If resection becomes imperative because of coexisting pathological process, the surgeon must decide whether a one stage or two stage procedure is indicated. In fact, the principles governing bowel resection in general should be closely adhered to.

**Prophylactic measures.** If reduction has been accomplished and examination of the gut shows no presenting pathological condition, there remains only the consideration of the means of preventing recurrence. In ileocecal involvement, the surgeon may perform a cecopexy or may suture a short section of ileum to the lateral wall of the cecum in an attempt to effect a mooring of the bowel. Bayard, in a paper dealing with intussusception of the sigmoid, which he states is the most common site of chronic intussusception, describes the following procedures for the prevention of recurrences: (a) plication of an excessively redundant mesentery; (b) suture of the longitudinal striae to the psoas fascia, (c) elevation of the pelvic peritoneal floor and obliteration of the pouch of Douglas by placing fascia lata strips across and beneath the peritoneum and attaching them to the pelvic brim on either side. These measures may be worth-while if no tumor is present. If, however, tumor is present, which is usually the case in this region, resection or exteriorization with secondary closure will be necessary and this will be sufficient to prevent recurrence. Some surgeons feel that preventive measures should not be attempted (28).

#### CASE REPORT

On December 16, 1939, H. F., a 28 year old male, was admitted to the Haverhill Municipal Hospital with a history of having had dull, cramp-like, periumbilical pain off and on for the preceding 11 months. During the preceding month he had had daily nausea and pain which would awaken him every morning and this pain would frequently last all day. At times the pain consisted of a constant dull ache and the patient said he never felt com-

pletely free from it. The past history was not significant except that appendectomy had been performed 14 years previously.

On the day of admission to the hospital, the patient was awakened at six o'clock in the morning with severe, constant, periumbilical pain which became progressively worse, and was accompanied by nausea and vomiting. Physical examination revealed nothing of significance with the exception of marked tenderness in the right side of the abdomen, most prominent in the mid third, and a definite mass in the same region lateral to the old appendectomy scar. There was a moderate degree of spasm present throughout the right side of the abdomen. Peristaltic sounds were not heard on auscultation. The mouth temperature was 97.4 degrees F. The pulse rate was 80. The blood pressure reading was 110/60. The white blood cell count was 21,800. A diagnosis was made of strangulation obstruction, involving the lower ileum, probably due to adhesions.

Laparotomy revealed a large mass involving the cecum and ascending colon as far as the hepatic flexure. The cecum was edematous and contained an intussusception of the ileum. An attempted reduction was made by applying manual pressure over the apex of the intussusception while gentle traction was exerted on the proximal ileum. This procedure was of no avail. A finger was then inserted at the neck of the invagination in such a manner as to dilate it sufficiently so that a finger could be passed along the side of the intussusceptum. When this was done it was found that the intussusceptum was spirally twisted. Alternate maneuvers of unwinding and applying traction led to the reduction of the intussusception which proved to be of the ileocolic type. Approximately 3 feet of ileum were involved in the process. This segment of ileum was dilated, pale, and moderately edematous. Careful palpation of this section of bowel revealed no tumors, diverticula, or other conditions which might have been responsible for the occurrence of the process. A few adhesions were found between the cecum and the parietal peritoneum and also between the uninvolved ileum and the peritoneum, but none of these adhesions appeared to play any part in the etiology of the condition. The ileum was replaced in the abdominal cavity and no further operative procedures were attempted.

The patient made a normal convalescence and was discharged from the hospital on December 30, 1939, feeling well.

In the 14 months which have elapsed since the operation he has had no symptoms referable to the intestinal tract.

#### SUMMARY

Varieties of adult intussusception are reviewed, and various therapeutic procedures are discussed. A case of adult intussusception which was apparently idiopathic is presented.

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# THE TERMINAL COMMON BILE DUCT AND DUODENAL PAPILLA

## A Roentgenological Consideration

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**I**N the routine roentgenological study of the duodenum, many anatomical changes occur in the ampullary segment. Although these changes seemingly are of scant importance, they are of inestimable value in the diagnosis of pathological conditions. The literature pertaining to roentgenology and textbooks on the use of the roentgen-ray in gastrointestinal disease pay scant attention to the interior of the descending duodenum, and very little is mentioned regarding the roentgenological criteria of affections involving the terminal common bile duct and the duodenal papilla. There seems to be a lack of knowledge regarding the roentgenological manifestations of disease of this segment of the bowel, which no doubt accounts for the paucity of information.

Recent roentgen-ray investigations of the interior of the digestive tract have contributed considerable information regarding the earlier manifestations of pathological conditions. A study of the roentgenological appearance of the normal interior of the ampullary portion of the duodenum has been presented in a previous communication (1), is of invaluable aid in determining the presence of disease in this segment. Although minimal changes occurring in this portion of the duodenum often challenge the acumen and vigilance of the roentgenologist, a discussion of these changes will no doubt lead to a better understanding and improvement in the diagnosis of diseases affecting this portion of the bowel. As a result of the confusion and lack of knowledge of the roentgen-ray picture produced by the various diseased processes involving this region, minimal or early changes in the mucosa and the contour of the duodenum have been given little consideration. The necessity for a roentgenological investigation of the ampullary segment of the duodenum has therefore become increasingly important, due to the fact that the majority of cases of disease of the terminal common bile duct and papilla are either misinterpreted or not recognized. However, a re-study of roentgeno-

grams of many proved cases of disease of this segment has shown that there were distinct, demonstrable, minimal changes which were not recognized at the time of the roentgen-ray examination. Failure to recognize abnormalities in the ampullary portion of the duodenum is in part due to lack of knowledge of the roentgen-ray criteria of diseases demonstrable in the interior of the duodenum.

The descending portion of the duodenum is of especial interest because of its relation with the terminal common bile duct, the papilla, and the head of the pancreas. It must be strongly emphasized that lesions involving the terminal common bile duct or the duodenal papilla invariably affect the duodenum, either by invasion of the lesion or by producing a pressure defect upon the configuration of the mucosa or its exterior contour.

In this communication the normal roentgen-ray appearance of the interior of the ampullary portion of the duodenum will be briefly discussed, and the anatomical changes occurring in the mucosa, papilla, and terminal common bile duct considered. The roentgenological picture of the duodenum is ordinarily a relief of the interior. Normally the transit of the barium meal caudad through the duodenum is very rapid, but it is rarely empty as long as the barium is being expelled from the stomach. Some barium nearly always remains in the duodenum long enough to obtain a view of its interior and contour. Serial roentgenograms, presenting views in different stages of filling and emptying of the duodenum are essential for the proper investigation of the ampullary portion. By the utilization of the fluoroscope, large gross lesions can easily be detected. Changes in the mucosal folds, the demonstration of the papilla and other minute findings are best observed in serial roentgenograms, preferably without compression, although at times compression is useful in delineating the pathological process. The normal mucosa of the interior of the descending duodenum is portrayed by transverse circular folds known as Kerkling's folds. These folds project into the lumen, consist

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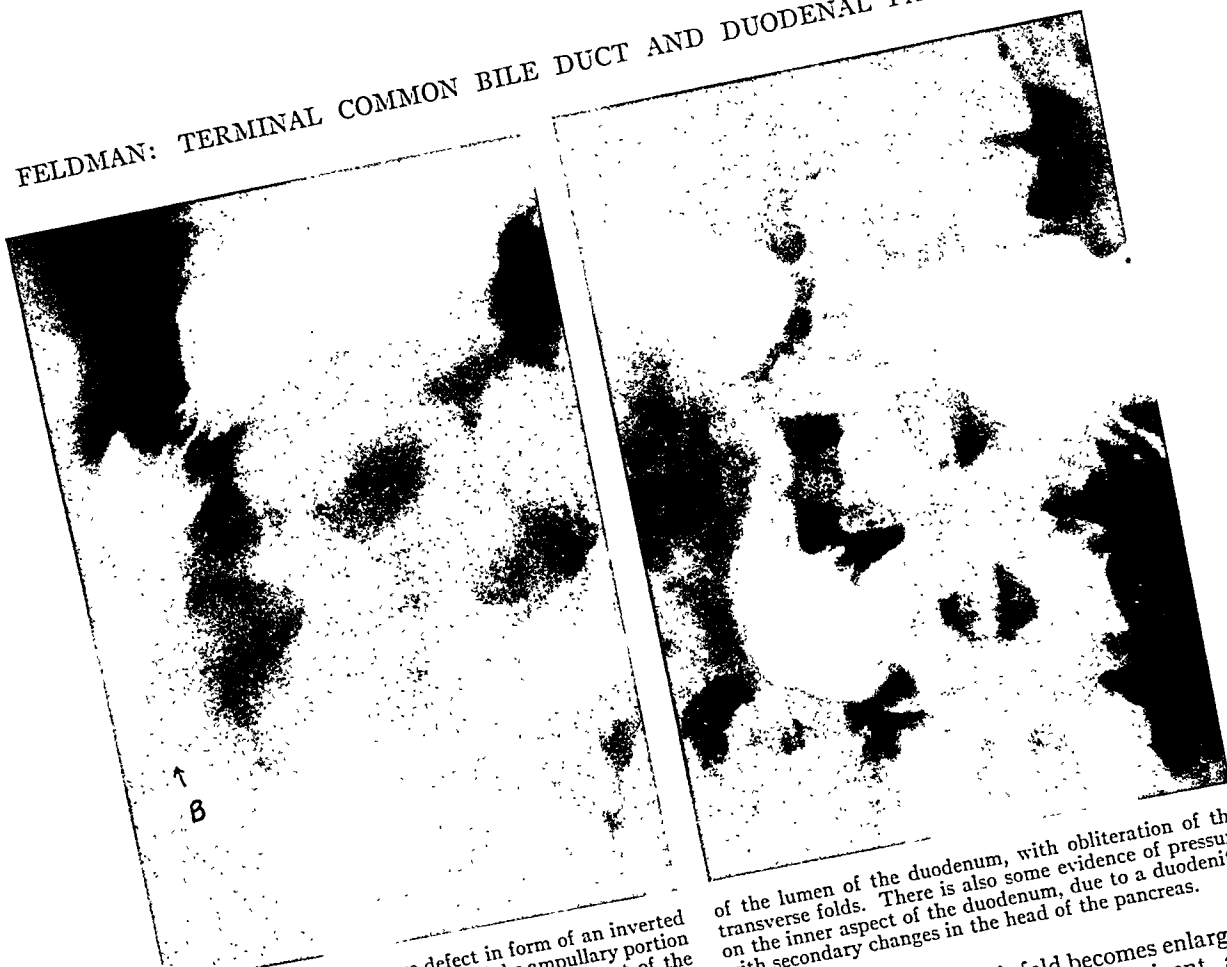


Fig. 1. a, left, A pressure defect in form of an inverted three is shown on the inner aspect of the ampullary portion of the duodenum at arrow A. Slight enlargement of the duodenal papilla is shown at arrow B. Right, A narrowing

of the lumen of the duodenum, with obliteration of the transverse folds. There is also some evidence of pressure on the inner aspect of the duodenum, due to a duodenitis with secondary changes in the head of the pancreas.

not only of the mucosa but also of a supporting submucosa and do not disappear under compression.

The ampullary portion of the duodenum at the juncture of the posterior and left wall reveals a slight elevation projecting into the lumen, which is produced by the traversing common bile duct. Over this area is seen a low longitudinal fold known as the plicae longitudinalis duodeni. This fold is interrupted by the duodenal papilla, but continues below the papilla for a short distance. The latter fold normally varies from 4 to 6 centimeters in length and from 2 to 4 millimeters in width. At its beginning it is shallow, but becomes more prominent as it approaches the papilla. Roentgenographically it produces a single longitudinal narrow negative shadow. Occasionally this fold may be demonstrated in the normal subject; however, it is more often portrayed in affections involving the terminal common bile duct. In the early stages of disease of

the common bile duct, this fold becomes enlarged, thickened, broadened and more prominent, and produces more or less characteristic mucosal changes in the interior of the duodenum. In later stages, changes in the contour of the duodenum, as well as varying degrees of stenosis, are often demonstrated.

The bile papilla or major duodenal papilla projects into the lumen as a prominent nipple-like process, through which the biliary and pancreatic ducts usually empty. The roentgenological demonstration of the normal major duodenal papilla has likewise received little attention. The papilla can be demonstrated in many instances in the mucosal relief view of the interior of the duodenum. The normal papilla roentgenologically presents itself as a small rounded, more or less circular negative shadow, varying from 3 to 5 millimeters in diameter. It has the appearance of a punched out hole. Occasionally a hood-like semicircular fold may be seen atop the papilla.





Fig 2a

Fig 2 a, A punched out defect is shown at arrow B, in the upper descending duodenum in region of the minor papilla. A broad longitudinal fold is observed extending below this defect. There is some compression of the inner aspect of the ampullary portion of the duodenum, due to pancreatic pressure. Note the ragged appearance of the

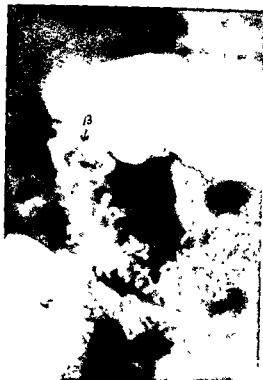


Fig 2b.

contour of this segment. b, Same case. A large negative shadow is demonstrated at arrow B similar to the defect in the opposite roentgenogram. The defect simulates a polyp, but since it is continuous with the longitudinal fold it is probably an enlarged minor papilla. Contour of descending duodenum is ragged due to inflammatory changes

Close inspection of the mucosal contour of the papillary area may at times reveal minute changes that are indicative of early pathology. Any enlargement of the size of the papilla must be carefully studied for early pathological manifestations. The enlargement varies according to the stage of the disease. In late cases it may become large enough to produce changes in contour of the duodenum and varying degrees of stenosis.

Anatomical changes produced by inflammatory affections cause swelling in the ampullary area, papilla, and terminal common bile duct. Benign and malignant tumors will produce changes which are chiefly manifested in the wall of the duodenum, causing definite contour change as well as changes in the configuration of the mucosa. Although clinical and roentgenological data are often deemed to be adequate to sustain the diagnosis of a pathological condition, the similarity of roentgen ray findings frequently makes re-

sults difficult to interpret accurately. A histological roentgen-ray diagnosis cannot always be made with certainty. However, since the most conspicuously affected portion of the duodenum is isolated to a small segment surrounding the papilla, careful clinical and roentgenological studies will often lead to a correct diagnosis. It has frequently been stated that lesions of the terminal common bile duct and papilla cannot be diagnosed by means of the roentgen ray. However, one should correct this impression, for it is believed that a large percentage of cases can be correctly diagnosed when attention has been focused upon this segment of the duodenum. Numerous isolated proved cases of pathological affections of the terminal common bile duct, have been gathered from the literature to corroborate the roentgenological criteria which are established in this presentation. The roentgenological data are further strengthened by the numerous autopsies

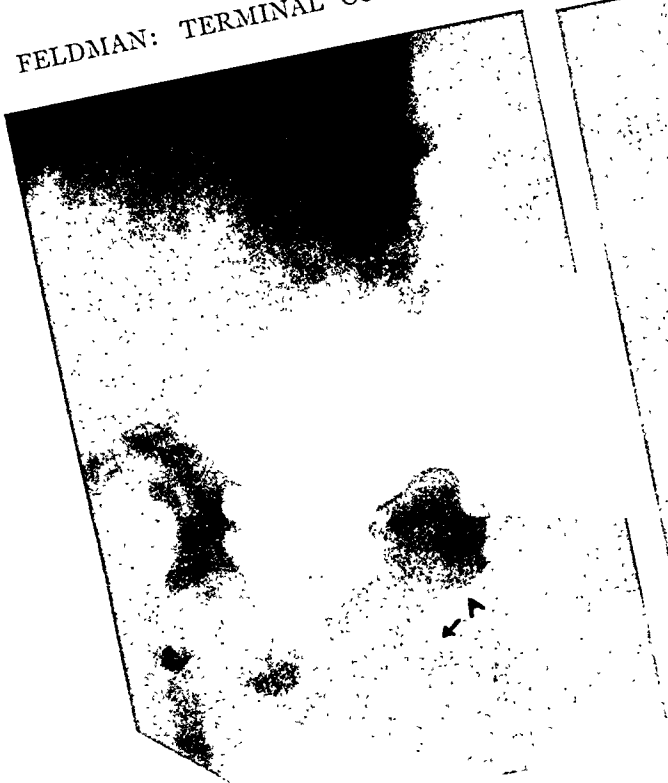


Fig. 2c.

Fig. 2. c, Narrowing of the duodenum is illustrated in the same case and also compression from the head of the pancreas is shown at arrow A. d, Same case, oblique view, narrowing of the lumen of the duodenum is shown at



Fig. 2d.

arrow A. The longitudinal fold is not seen in this position, except at arrow B, where a short longitudinal fold is seen below the region of the major papilla. An ulcer niche defect is shown in the duodenal bulb at arrow C.

and surgical observations. Impressive cases of carcinoma of the common bile duct have been described in the more recent literature and have revealed roentgenological changes that are more or less diagnostic. Notwithstanding the fact that it is often stated in the literature that the routine gastrointestinal roentgen-ray examination yields little information regarding pathological changes in the terminal common bile duct, the failure to diagnose such cases cannot be charged altogether to roentgenography, but rather to a lack of experience and knowledge of the roentgenological criteria produced by diseases affecting the ampullary segment of the duodenum. Since the terminal common bile duct and papilla are closely related to the duodenum, and since most lesions involving them encroach upon the lumen, they must in some way produce anatomical changes which should be recognized by means of the roentgen-ray. When lesions ulcerate or when stenosis occurs the pathological change should be

quite characteristic. It must be borne in mind, however, that at times it is very difficult to evaluate slight departures from the normal.

The following roentgenological signs may be observed in affections of the terminal common bile duct and the major duodenal papilla: (1) enlargement and broadening of the plicae longitudoinalis duodeni fold, (2) encroachment of the enlarged duodenal fold upon the lumen of the duodenum, (3) mucosal changes surrounding the longitudinal fold and changes in the pattern of the ampullary mucosa, (4) enlargement of the major duodenal papilla, (5) filling defect in the contour of the duodenum, (6) varying degrees of stenosis, (7) secondary ulceration producing a defect, (8) invasion of the pancreas which may produce signs of pancreatic pressure on the contour of the duodenum, (9) cholecystographic changes, producing nonfilling of the gall bladder when the bile duct is occluded, (10) pressure defect of the stomach in late cases.



Fig. 3 Roentgenogram illustrating a wide longitudinal fold at arrow B. An enlarged papillary negative shadow is shown at arrow A. Note the ragged contour of the upper portion of the descending duodenum, due to inflammatory changes.

Inflammatory conditions of the terminal common bile duct roentgenologically present a thickened, broadened plicae longitudinales fold and also enlargement of the papilla. The transverse folds are shortened as a result of the projecting swollen longitudinal fold into the lumen. There are often secondary inflammatory changes involving the duodenum, producing a characteristic picture of a duodenitis, with narrowing of the lumen, and changes in the mucosal picture of the duodenum.

In carcinoma of the terminal common bile duct and papilla, the fold is enlarged in varying degrees, according to the stage of the disease. In the early stages the findings are similar to those caused by an inflammatory process, but in later stages the fold becomes quite large, prominent, and persistent, and produces a marked encroachment upon the lumen with a filling defect in the contour of the duodenum. There are also changes

in the mucosal pattern denoting a neoplastic lesion. The papilla frequently becomes enlarged, producing a filling defect of an intraluminal duodenal lesion. The defects resulting from the enlargement of the longitudinal fold and that of the papilla are portrayed roentgenographically as negative or translucent areas displacing the barium. The caliber of the lumen is narrowed in varying degrees. In lesions involving the common bile duct alone, the defect is usually smooth and sharply outlined. When the duodenal wall is invaded the defect is quite irregular. Lesions involving the papilla produce a defect simulating a polyp. The defect is usually smooth, but in later stages it becomes irregular as the duodenal wall is invaded. Stenosis of the duodenum is usually a late manifestation and frequently indicates duodenal invasion. The degree of stenosis varies, but it is rarely complete. In benign obstructive lesions there may be some dilatation proximal to the lesion, while in malignant conditions the lumen reveals no dilatation. In late stages, especially in carcinoma, it may be very difficult to differentiate a primary duodenal lesion from that of a primary common bile duct or papillary lesion.

In benign tumors of the papilla, the size of the papillary defect is considerably increased, depending upon the size of the tumor. Roentgenologically the lesion is depicted as a smooth, rounded enlargement in the papillary area producing a large sized negative defect, simulating a large hole.

Stones in the terminal common bile duct cannot as a rule be demonstrated in the relief roentgenograms of the interior of the duodenum, unless the stones contain an excess of calcium.

Ulceration when present can be shown at times surrounding the common bile duct area, by the crater produced. Recognition is difficult, since its crater is often shallow; but changes in the mucosal pattern may give a clue to this condition.

The mucosal pattern of the interior of the duodenum invariably shows some demonstrable changes in its configuration. In neoplastic diseases the mucosa is either obliterated or displaced in the affected area. The break in contour of the normal transverse folds is readily shown in serial roentgenograms. Large lesions are ordinarily seen under the fluoroscope. As the plicae longitudinales duodeni fold becomes enlarged, the transverse folds are displaced laterally, so that in the roentgenograms the transverse folds are not continuous folds, but seem to end abruptly at the enlargement. A similar picture is seen in the region of the papilla, where the transverse folds may be shown to be displaced and obliterated by the encroaching tumor mass.



Fig. 4. a, left, Anteroposterior view is shown of a proved case of carcinoma of the terminal common bile duct, demonstrating an annular defect. b, Same case, oblique view.

The irregular contour of the duodenum and also the slightly widened longitudinal fold are shown at arrow A. (Case of Dr. Samuel Brown, Cincinnati.)

Tumors originating in the duodenal wall, roentgenologically simulate those occurring in the papilla. However, tumors originating within the terminal common bile duct have several characteristics by which they can be differentiated from those of the duodenum, especially in the early stages of the disease. Malignant tumors of the duodenum are more often an infiltrating or a polypoid lesion which originates in the interior of the duodenum and cause stenosis much sooner than those originating in the duct. Those occurring in the duct produce early biliary symptoms, while those occurring primarily in the duodenum produce secondary gastric disturbances in the early stage, and when biliary symptoms occur, these are late manifestations. In the later stages of disease involving the common bile duct and the papilla, when the duodenum has been invaded, it is then difficult for the roentgenologist to determine the exact origin of the tumor. This also holds true for the surgeon, when exploration is made.

In carcinoma of the terminal common bile duct, the contour of the external duodenal curve is not

affected and there is no displacement of the duodenum. The defect is often sharply outlined. The plicae longitudinales duodeni fold is enlarged, and thickened. The major duodenal papilla may also be enlarged. The mucosal pattern is distorted and the mucosa is displaced. There is frequently some degree of encroachment upon the lumen; although it is very slight in the early stages of the disease, it may become very marked in late instances, when there may be varying degrees of stenosis. When stenosis occurs the defect is annular and smooth, but is often irregular in later stages. Occasionally ulceration or secondary changes in the pancreas may be observed.

The effect of lesions of the terminal common bile duct and papilla upon the pancreas is roentgenographically less striking. Not infrequently however, the pancreas is invaded in cases of carcinoma or there may be some swelling of the head of the pancreas secondary to duodenal affections which produce characteristic roentgen-ray changes in the contour of the duodenum. This is evidenced by the slight pressure upon the inner aspect of the ampullary portion of the duodenum, producing an inverted three defect (2).

The effect of lesions of the terminal common bile duct and papilla upon the cholecystographic study of the gall bladder is quite obvious. There is frequently a nonfilling of the gall bladder, though there may not be any actual anatomical disturbance of this organ. The gall bladder may be faintly visible on the flat film in some instances as a result of an empyema following biliary obstruction. A normal gall bladder may be dilated and visible on the plain roentgenogram. In some cases in which the obstruction is incomplete, the dilated gall bladder becomes visible following the administration of dye. The association of gall stones in cases of terminal common bile duct pathology occurs less frequently than in cases of other biliary diseases.

In affections of the upper common bile duct, proximal to its entrance into the duodenum, there may be evidence of pressure upon the adjacent structures, such as caused by carcinoma, or dilatation of the common bile duct due to other conditions. It may produce a pressure defect upon the duodenal bulb or superior duodenum, or upper portion of descending duodenum. In rare instances in the presence of a duodenal diverticulum, a pressure defect may be seen in the diverticulum.

The clinical features of intrinsic obstruction of the common bile duct are almost indistinguishable from those produced by extrinsic pressure, such as from carcinoma of the head of the pancreas. There are, however, several clinical differences which should be considered. In the case of intrinsic bile duct obstruction, there are few constitutional symptoms at the onset. There is usually pain following the sudden onset of obstruction. The symptoms simulate those of common duct stones. On the other hand, obstructions due to extrinsic pressure are usually painless. Of especial interest is the fact that lesions involving the terminal common bile duct and duodenal papilla give rise to symptoms very early in the course of the disease. Jaundice usually occurs at an early period and is the predominant objective sign. The clinical diagnosis of biliary

obstruction is usually quite obvious, but the exact site and the nature of the pathological process is difficult to determine. However, a complete and thorough roentgen ray investigation of the gastrointestinal tract and gall bladder may disclose the site and often the etiological condition. In obstructions of the common bile duct, there is usually a dilatation of the common bile duct and gall bladder, with enlargement of the liver as a result of biliary stasis.

#### SUMMARY

Minimal roentgenological changes in the contour and mucosal pattern of the ampullary portion of the duodenum are shown to represent pathological conditions. Many pathological affections involving the terminal common bile duct and major duodenal papilla are often overlooked in the early stages. Occasionally some abnormality is recognized but is often difficult to interpret because of lack of knowledge of the early roentgen-ray manifestations of disease that occurs in this portion of the duodenum. Roentgenographical changes in the ampullary segment are emphasized as a point of origin for the majority of lesions occurring in the duodenum, exclusive of the duodenal bulb. The roentgen-ray investigation offers the best means to diagnose correctly affections of this portion of the duodenum. A number of facts stand out pre-eminently in this study, namely:

1. The basic roentgen-ray criteria of the normal interior of the ampullary portion of the duodenum are reviewed.
2. Changes in the normal mucosal pattern are discussed.
3. The roentgenographical criteria of pathology of affections of the common bile duct and major duodenal papilla are described.
4. Diseases involving the terminal common bile duct and papilla invariably produce some changes in the duodenum.

#### REFERENCE

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# FERRULE CAPS FOR THE HEAD OF THE RADIUS

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CERTAIN fractures of the head of the radius may lead to surgical removal of the head if there is resulting distortion of the rounded articular surface from fragmentation and comminution, especially when there is displacement of fragments, some of which may penetrate through the joint capsule completely. Necessity for this operation may also arise in the complications after fracture of the ulna or dislocation of the radius or of both bones at the elbow. Delayed causes leading to desire to remove the head may be found in excessive new bone formation about the head and into the elbow joint or surrounding tissues ending in loss of pronation and supination or interference with full flexion and extension of the forearm, partial or complete bony ankylosis of the elbow joint, painful joint containing loose or attached osseous bodies, or interference with the radial nerve from local pressure or callus inclusion.

The necessity for removal of the head of the radius develops most frequently in adults—very seldom, if ever, in children. Some of the delayed causes may be traced to too early active or passive movement of the elbow joint and a failure to immobilize fractures considered to be lacking in sufficient osseous damage to warrant primary excision of the head of the radius. In the course of healing after fracture, during a convalescence of permitted movement, no immobilizing splint having been employed, new fibrous tissue and new bone easily overdevelop, which process may terminate in shrinking of capsular capacity, fixation to surrounding structures, ankylosis of the joint in part or completely, and setting up of severe pain with dysfunction. Such results often follow a failure to comprehend the nicety of the rotatory mechanism supplied by the superior radioulnar articulation and its basic importance in the acts of pronation and supination of the forearm. In the adult, this close-fitting rotating joint will not tolerate much irregularity on its articular surface without functional impairment. Consequently, resection of the radial head and neck proximal to a point where it becomes extra-articular may avoid many complications within the joint leading to impaired function.

All operations described in this article have followed my continued practice of limiting the procedure within the joint, not cutting the orbicular ligament nor injuring the radial nerve. To accomplish this the resection must be accompanied by gentle removal of all osseocartilaginous fragments, whether loose or attached, by a straight cutting off of the neck without leaving projecting bone spicules, and by a minimal amount of irritation and damage of the synovial surface and of any part of the surrounding joint structures. For many years also I have advocated closing over the resected open neck of the radius with pieces of periosteum, or nearby soft parts of transplanted fascia. On the other hand, much of the limitation of elbow joint motion after these injuries can be traced to periarticular fibrosis and thickening of the capsular structures set up by the tearing and hemorrhage of the primary injury or subsequent irritation from unwisely forced movements in the presence of distorted bone fragments.

Following simple removal of the head and closing of the joint, the forearm may be flexed in full supination to approximately 80 degrees with the arm and held there by a suitable plaster-of-Paris splint from the base of the fingers to the axillary margin which immobilizes the joint and precludes any rotation of the forearm. Such a splint must be worn until the hemorrhage into the joint and surrounding tissues, the combined result of fracture and operation to remove the head, has been absorbed. Motion after a too early freeing from splint support may merely lead to an increased restriction of function. This splintage may last as long as 6 to 10 weeks. Thereafter, as healing is controlled by x-ray examination in an endeavor to eliminate the possibility of new bone formation, application of local heat and active use short of pain may be helpful in curtailing convalescence and hastening functional return.

The cut-off neck may then round out and cause no local joint restriction, or it may perversely lead to local new bone and fibrous tissue formation and restriction of joint motion. In addition to these local changes, the loss of the head and part of the neck of the radius after removal may affect the distal radioulnar joint by permitting the radius to foreshorten in its longitudinal axis in spite of the support of the interosseous ligament between the two forearm bones. This possibility may follow

in the cavity quite perfectly to maintain full length of the radius without demonstrable injury to the cartilage over the capitellum humeri. Under conditions of accurate apposition of the cap, rotating motion of the radius on the ulna was preserved. And in most instances, even after 7 months' burial in the joint, the articular surface of the ferrule remained free from binding adhesions and in no instance showed intra-articular bands or adhesions to the humerus. The greatest degree of overgrowth of tissue was represented by a thin, pellicle-like, membranous structure, grossly resembling regenerated synovial tissue.

Regardless of accuracy and holding character of fixation, all ferrules became aseptically covered after formalin fixation by a thin, precipitated albumin from the synovial fluid of the joint and tended to become filled with soft, gelatinous granulation tissue, which even in the specimen with cap buried over 7 months (dog 1) showed no tendency to fibrous thickening. When the caps were of the slit type, this tissue within tried to grow out through the slits and unite with the advancing overgrowth of fibrous tissue regenerating from the joint covering.

In contrast, when the head was removed by similar technique and subjected to an equal chance for active use after operation, the control joints of the same dog became the seat of a greater outgrowth of bone which tended to re-form and simulate the removed head in contour. This did not, even in dog 1, 7 months' duration, grow out to full size of the head of the radius, nor did it fully occupy the surface of the joint which formerly held the head of the radius. These control joints showed also a greater amount of fibrous tissue overgrowth, some intra-articular adhesions, and a greater restriction of rotatory motion, in dog 1 amounting to a clinical bony ankylosis between radial neck and sigmoid notch of the ulna.

It was not possible to show in dogs that loss of length developed in the radii which were not supplemented by the ferrule after excision of the head, although the dog actively used the leg over long periods of time. The dog's forearm permits far less rotatory motion at the superior radioulnar joint than does a human elbow, and the two forearm bones are much more closely bound together by the powerful interosseous ligament. Supporting soft tissues including muscle and tendons are tougher and less voluminous, and the leg as a whole has far less proportionate amount of subcutaneous fat than the human forearm.

#### CASE REPORTS

**CASE 1** Mrs Isabelle C., 55 years old, fell May 1, 1940, and injured her right elbow. She was seen first on May 10,

1940, with clinical findings of fracture of the head of the right radius. The roentgenogram showed a comminuted head, angularly displaced at the neck, and a longitudinal split running down the shaft of the bone.

Operation to resect the head and implant the vitalium ferrule was performed on May 20, 1940, a Martin bandage being used on the arm. When the joint was opened, the comminuted head, still attached by a few narrow periosseal shreds, was seen at once to be angulated. The cartilage on the joint surface of the head was completely torn off and lay between the two major bone fragments. The ferrule was fitted over the trimmed neck of the bone as well as could be done, and it was attached by a catgut suture inserted through a drill hole in the bone and tied through the opening in the metal cap. It did not fit very well, as the aperture in the cap was too small. This was one of the first type of ferrules made.

After the wound was closed, no splintage of any kind was employed, but after the forearm was dressed it was held in a sling at right angles to the arm, and active motion was encouraged from the second postoperative day. The wound healed cleanly. The patient left the hospital in 7 days with instructions to continue use short of pain. By June 24, 1940, she could do her regular housework, could extend her forearm to 140 degrees with the arm, and had very slight, if any, pain in elbow. Supination was possible only to a straight line, pronation was three fourths normal. This condition improved a little, and she kept on using the arm.

On November 7, 1940, flexion of the forearm was normal extension within 8 degrees of normal. A roentgenogram showed that the ferrule had been displaced away from its seat on the upper end of the radius but still lay in the cavity of the superior radioulnar joint, and that some new bone had formed around the end of the cut-off neck of the radius. There was no pain in the distal radioulnar joint and no evidence of anatomical disturbance of it shown by roentgenological examination, as might follow shortening of the radius.

She re-entered the hospital December 3, 1940, and a second operation was performed the following morning, an entrance being made into the joint via the old scar, which was excised. When the elbow joint was opened a small amount of normal colored synovial fluid was encountered. There was some periarthritic fibrosis in the tissues, but the cap was completely enclosed within the joint, and the synovial surface about it was in no place adherent. Its surface was smooth and shiny as on the day of implantation 7 months before, and it lifted out with ease. Around the neck of the bone was some newly formed osseous tissue and a contracting, soft, osteoid mass plugging the medial lary canal of the bone, which dissected off easily. The neck and newly formed bone were chiseled off quite squarely, and the last made type of ferrule with projecting pin was quite satisfactorily slipped over the bone end after insertion of the point in the slightly reamed out medullary opening. The joint was closed completely and dressed, with no splintage. On December 19, 1940, the wound was completely healed. There was much freer and painless flexion and extension and rotation a little beyond a straight line in supination. This result was much more satisfactory.

The findings in this patient, in whom a misplaced ferrule was removed and replaced by a pin extension ferrule after 7 months, indicate that the human elbow tends to react with less fibrous tissue regeneration than in that of the dog. Her elbow joint showed no intra-articular adhesion, and the ferrule was completely covered and lay within the

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joint space, from which it was readily lifted after the scar of original operation had been opened. This was in marked contrast to the findings in dogs, in which the head had to be pried out even though buried only a month.

I have seen in roentgenograms a shadowy outline of apparent regeneration of the head of the radius developing within a year after I have surgically removed the head of the bone. No opportunity has ever been given to study the character of the material causing this shadow, nor to determine whether it resulted from regeneration from the cut-off neck or represented a deposit of calcified material in the wall of that portion of the joint immediately overlying the site of the removed head. Similar regrowths have been reported by Sutrow.

CASE 2. Frank F., 21 years old, shipping clerk, was first seen August 29, 1940, when he fell about 8 feet to a brick pavement with resulting fracture of the left carpal navicular and head of the right radius, along with dislocation of the right ulna at the elbow. The dislocated joint was reduced. On August 31, 1940, the right elbow joint was opened, a Martin bandage being used on the arm. As the superficial tissues were cut through, local edema was encountered, and when the joint was opened, bloody synovial fluid ran out, and the fractured head of the radius appeared. It was lifted out, the joint searched for any small fragments, and the neck was cut off quite squarely about  $\frac{3}{4}$  inch back from the normal joint ends, the procedure keeping within the elbow joint and avoiding injury of synovial surface and capsule except at the site of entrance incision. Over the end of the radius a vitallium ferrule was quite well fitted and was held in position without suture or additional fixation. The joint was closed, and on account of the recently reduced dislocation of the ulna, the forearm was held at right angles to the arm in full supination in a posterior molded splint, carried in a sling.

A few days later we were able by fluoroscopic examination to make additional diagnosis of a duodenal ulcer and a long retrocecal appendix in this patient following a small bowel hemorrhage. By September 10, 1940, there was good painless rotatory motion in the right forearm. The wound was healed, and the stitches were removed. He was allowed to leave the hospital without splintage on the right arm and was instructed to attempt such active use as caused no pain. On December 17, 1940, he had about 15 degrees of supination beyond the midline and nearly complete flexion. Full extension of the forearm lacked about 12 degrees. There was no great complaint of elbow pain. However, there was a feeling of crepitus when the forearm was rotated, and the thumb pressed over the imbedded cap. Roentgenographic examination showed the cap angled and not on the neck very well. There was a little bone growing up over the ulnar surface of the cap but no excess new bone developing around the head of the radius. There was no disturbance in the distal radioulnar joint.

CASE 3. George H., 31 years old, packer, was first seen on November 1, 1940, and stated that 3 weeks before he had fallen, broken his right elbow and had been treated by the application of a posterior molded plaster-of-Paris splint directly upon the skin, extending down the arm and forearm to the wrist with the forearm in a position of 100 degrees extension with the arm and in slight pronation. This splint was removed with some difficulty, and a roentgeno-

gram showed a fracture of the right olecranon almost at its base with the shaft of the ulna pushed forward and a comminuted fracture of the head of the radius. On account of the condition of the skin about the elbow, operation had to be deferred until November 6, 1940.

After application of a Martin bandage, an incision was made on the outer side of the elbow starting just above the external condyle of the humerus extending down along the shaft of the radius. This was deepened to the elbow joint from which bloody joint fluid escaped. The head of the radius was visualized and was found to be comminuted and severely broken. The fragments were removed, the neck of the bone was smoothed off, and a vitallium cap was inserted with the center pin projecting into the medullary cavity of the bone. A quite snug fit and accurate application were obtained. This incision was closed with catgut in layers and with black waxed silk in the skin. A second incision was made starting near the end of the olecranon process down the shaft of the ulna, which exposed the fracture just below the elbow joint. The fragments of ulna were brought into line, and on the posterior surface was applied a four-screw vitallium plate, which held the main fragments in good alignment but was unable to grasp the intermediate triangular fragment very satisfactorily. This wound was applied from just below the axilla to the base of the fingers with the forearm at right angles to the arm and in full supination.

On December 17, 1940, the plaster was removed; the wounds were cleanly healed. There was little power of pronation or supination. Roentgenogram showed the cap properly in place on the radius. The ulna showed no callus. The arm therefore was replaced in a circular plaster-of-Paris dressing from the base of the fingers to the axilla at right angles to the arm and in supination. He later developed union in the ulna and now has about 50 per cent functional use of the joint.

A question yet to be decided is whether some period of immobilization in a suitable splint is better after application of the metal cap or whether early motion should follow. Will the early motion lessen the amount of joint shrinkage and confining periarticular fibrosis? Apparently the protecting cap does not tend to adhere to the lining of the joint in human beings. It easily and quickly becomes surrounded by a normal appearing synovial surface and of itself causes no pain or distress even when not tightly affixed or adherent to the shaft of the radius. This observation is different from the amount of heavy fibrous enclosure of the ferrule observed in dogs. The ferrule probably does, however, require firm fixation to the end of the radius to display its best effects. It may not require the approximately full size nor the normal anatomical configuration of the head of the radius but may be smaller in circumference than the resected head and easier to insert on that account. It must, however, maintain the anatomical length of the radius.

Apparently the cap should be fitted with a central pin for insertion into the medullary opening of the head of the radius to give both fixation and axial alignment. It should likewise not be



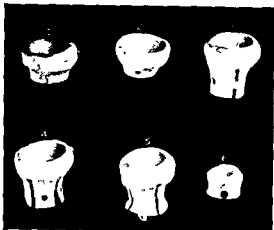


Fig. 1. Evolutional series of vitallium caps used for replacement after resection of head of radius. 1, Resected normal head of human radius. 2, First type of ferrule cap with small holes for suture or nail insertion to fix onto shaft. 3 and 4, Caps with longer and slit skirts, permitting adjustment at time of operation for purpose of slipping over neck of radius. 5, Final type of cap used with center pin, which can be inserted into medullary canal of bone (Fig. 2). 6, Cap used for experimental work on dogs, the final model with center pin not shown here.



Fig. 2. Postoperative film showing ferrule cap with center pin placed accurately on the neck of the radius with sufficient space between it and the condyle of the humerus. The small vitallium plate holding the ulna has failed to grasp the intermediate fragment completely, but alignment is satisfactory. This went on finally to bony union and about 50 per cent recovery of full function.

when the ligaments at the wrist have been in some measure disrupted at the time of the original injury without full clinical evidence of fracture or dislocation of the head of the ulna or even looseness of the distal radioulnar joint, because the surgeon overlooked this in considering the all too evident damage of the structures in the elbow joint. Shortening of the length of the radius may disarrange the distal radioulnar joint, upset the normal relationship of the two styloid processes at the wrist, and bring the normally more distal radial styloid back to the horizontal level of the ulnar styloid or further, when viewed in the roentgenogram. The patient's honest efforts to increase the range of rotatory motion at the elbow may add to this derangement by increasing vicarious function and irritation of the distal radioulnar joint, ending in painful wrist, lack of power, and some radial flexion of the hand with changed external appearance, characterized by undue prominence of the head of the ulna. Therefore, the more nearly an anatomically accurate filling in of the hiatus following removal of the head of the radius is obtained by any means, the more content the surgeon may feel that an important factor in the avoidance of undesirable after-results following this mutilating but sometimes necessary procedure may result. This factor is a close second in importance to the nicety of the resection of

the head without stripping of periosteum of the diaphysis, without spattering bone fragments and cells potentially osteogenetic into the joint or the periarthral tissues. This includes the squaring off of the end of the shaft fragment without splintering. The third important factor in treatment is rest in a supporting splint and sling for 4 to 6 weeks to permit quiet healing without new bone formation. The vitallium cap may overcome some or all of these difficulties.

A tentative attempt to overcome some of these disabling changes has been made by the use of vitallium caps or ferrules, which may be fitted down over the cut-off neck of the radius at the time of removal of the head or even at a later stage, when new bone formation or restriction of joint movement has occurred. Such a ferrule-like cap has been made from casts of resected normal heads of the radius. By the implantation of these metal replicas it was hoped that, after the joint had been gently cleansed of loose fragments, for the broken or fragmented head could be substituted a nonirritating and nonadhering body of exact shape of the original head which would permit rotation, prevent new bone formation, and in addition maintain complete length of the radius by a normal pressure against the external condyle of the humerus. Thus changes in the distal radioulnar joint subsequent to length loss of the radius and loss of support by impingement against the condyle of the humerus might be avoided. Likewise earlier active use of the elbow after resection

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of the head of the radius might be permitted without fear of new bone formation, excessive joint irritation, and subsequent adhesions or contractions. These factors taken together might lessen the period of convalescence and insure a higher percentage of functional recovery after lesions supposedly demanding removal of the head of the radius.

Substitute radial head ferrules were first prepared for dogs of medium weight, 15 to 18 pounds, from a cast made of radial heads obtained by operation. The first ferrules were hollow, polished, and were expected to fit quite exactly onto the resected neck of the radius, containing two or more perforations through which small fixation nails or absorbable stitches could maintain attachment to the radius. A second lot had split sides to permit greater ease in molding or bending to the variation in size of individual bones at the time of operation, and a third lot were made with extension center flanged pin for insertion into the medullary canal of the cut-off radius to afford both fixation and correct alignment. A similar revolutionary series of ferrule caps was prepared for use in human elbows.

### EXPERIMENTS

A series of experiments on dogs was performed. All dogs were operated upon under nembutal anesthesia, 1 grain to each 5 pounds of weight, by the use of strict asepsis and a constrictor on the foreleg. All dogs' wounds healed *per primam*. They were allowed all freedom of movement, without dressing, immediately after operation.

DOG 1, May 22, 1940, medium sized dog, weight 16 pounds. The head of the right radius was exposed, resected, and a vitallium cap was inserted into the hiatus. This fit fairly well over the upper end of the radius and on rotatory motions of the forepaw was seen to glide satisfactorily against the capitellum of the humerus. The wound was closed in layers with buried catgut and black silk in the skin. The head of the left radius was exposed and resected in a similar manner by the use of a chisel, and the wound was closed without the insertion of any foreign body. Both operations were performed with a constrictor around the upper part of the foreleg. No splints or dressings were used, as I wished the dog to walk on the legs as soon as possible and wished to permit all the irritation this would give.

DOG 2, July 18, 1940, the head of first one radius, then the other, was excised and a vitallium cap implanted in both defects.

DOG 3, September 5, 1940, the head of the left radius was resected and closed in the usual manner. The cap fitted very snugly and, to the best of my ability, in correct axis relationship.

DOG 4, November 12, 1940, the left elbow was opened and the head of the radius resected. The chisel unfortunately perforated the skin of the opposite side. One of the new caps with the projecting pin was applied. The joint was closed and the adventitious opening made by the chisel

was likewise sutured. The opposite right elbow was not operated upon.

DOG 5, November 15, 1940, a vitallium cap was applied on the head of one radius; the other head was removed and the joint closed without any further treatment.

*Summary.* December 11, 1940, all 5 dogs operated upon previous to this date are alive and well. Dog 1 shows no impediment whatsoever in walking. Dog 2 does not use the right forepaw quite normally. He holds it slightly flexed; while he will bear weight on it he will not extend it fully in jumping or playing. The others seem quite normal, especially dog 3, in which there is no evidence of any operative procedure. Dogs 4 and 5 play about without limp or evident distress in the elbow.

On December 11, 1940, the dogs were electrocuted. Examination after the superficial tissues were dissected away from the elbow region showed that all caps were thoroughly encased with fibrous, capsular tissue, and none were projecting out from the elbow joint through the joint covering.

The capsules of the elbow joints over the heads of the radii of dog 1 were split open and reflected so the head of the radius could be viewed clearly. On the capped side the shining, smooth surface of the metal cap remained in perfect condition, with a slight amount of free fluid in the joint and smooth synovial lining. There were no adhesions from bands within the joint. There was considerable if not a normal amount of rotatory motion in this capped radius. The second elbow, head of which radius had been resected but no cap inserted, was bony adherent to the ulna and would permit no rotatory motion (synostosis), although there was practically a normal amount of flexion and extension. There was no great amount of new bone formation around the head of the radius, but there were some intra-articular fibrous adhesive bands.

All elbows were then roentgenographed in an effort to portray the difference between the amount of bone formation on the uncapped and the capped side and any synostosis existing between the ulna and the radius in the uncapped or capped joint.

*Résumé of x-ray findings.* When the vitallium caps are well placed on the cut-off neck and hold position, the dogs being allowed freedom of exercise immediately after the operation, there is a minimum amount of new bone formation, not tending to overgrow the cap nor to invade the elbow joint. If the ferrule is not accurately applied, it tends to angle after active use of the limb, and bone rapidly develops along the exposed surface of the neck, tending to embrace and help fix the cap in the superior radioulnar space. When the cap is accurately applied and fixed in position with the center pin extension, although the medullary cavity has had to be opened, a minimum amount of new bone develops, and the ferrule fills

tinuous with a large mediastinal tumor. Crosby's case of thymic lymphosarcoma occurred in a 33 year old man who died 3 months after the first symptoms. The diagnosis was made at autopsy.

Symmers, Smith, Knutti, Evert, and Harvier regarded their cases as malignant, thymic lymphocytomas, basing their diagnosis on the situation of the tumor and its gross form. In other instances the thymic origin has been further supported by the presence in the tumor of cell groups resembling Hassall's corpuscles (Grandhomme, Helvestine, Coenen, Gerlach).

Very few of the reports on thymic lymphosarcoma contain information as to the reaction to radiation. Singer reported one such tumor which was highly radiosensitive. Janeway's 2 cases of thymic lymphosarcoma regressed under radium treatment but soon recurred. Repeated treatment kept one of his patients alive for 2½ years. In Harvier's case the tumor regressed readily under radiation but recurred so quickly that death resulted in 3 months.

Desjardin's patient was living, with disease still present, after 4 years. Haagenen reported 1 case of malignant lymphocytoma in an Italian boy of 14 years. Treatment with radium emanation was followed by regression of the mediastinal shadow. The fact that death occurred 5 weeks after radiation had been given, however, indicates that this presumed regression must have been very slight. Cutler reported 8 cases of thymic lymphosarcoma in 1935. In only 2 cases did the tumor respond to radiation. One patient was clinically free from disease 7 years after the onset. Another case was in good general condition 2 years after the diagnosis of lymphosarcoma was made.

#### CASE REPORTS

**CASE 1** Mrs. M. H., 61 years of age, white, married woman, was admitted to St. Francis Hospital, October 4, 1938. Three weeks before admission, the patient stated she had had pneumonia. Five days ago, she began to have shortness of breath which became progressively worse. She also noticed bloody sputum.

At the time of admission, the patient was cyanotic, and the breathing was rapid and forced. There was no swelling of the lymph nodes of the neck. The expansion of the thorax was limited on the right side and there was dullness to percussion and absence of breath sounds in the lower half of the right chest. The heart was moderately enlarged, the pulse rate was rapid, but regular. There was no edema. Roentgenological examination disclosed a dense cloudiness 3 inches (7.6 cm.) wide on the right border of the sternum, extending from the apex of the right lung to the diaphragm. After aspiration of about 1,000 cubic centimeters of thin, slightly bloody fluid from the right pleural cavity, the x-ray shadow was greatly reduced, and a diagnosis of mediastinal tumor was made. From the presence of lymphocytes and lymphoblasts in the sediment of the pleural fluid a tentative diagnosis of lymphosarcoma was made.

There was a short period of relief after the chest was tapped. Soon however, cyanosis, cough, and dyspnea became increasingly worse, and death occurred November 1, 1938.

Autopsy was performed and when the chest was opened, a large pyramidal mass, lying in the anterior mediastinum, came into view. The growth resembled the thymus in shape. The length was 18 centimeters, the width at the upper end was 6.5 centimeters, at the base 12 centimeters. It was firm in consistency and in color was pinkish-white. The mass was firmly attached to the pericardium, and the anterior surface of the heart was covered with a whitish 15 millimeters thick layer of tumor tissue. The right diaphragm was converted into a nodular hard mass, about 3 centimeters thick. The great blood vessels and bronchi in the upper mediastinum were firmly surrounded with the tumor mass. The right pleural cavity contained about 1,000 cubic centimeters of slightly bloody fluid.

The spleen was not enlarged and there were no tumor nodules noticed in the liver. The retroperitoneal lymph nodes formed a mass about 8 centimeters in diameter. In both kidneys several small nodules were protruding over the surface. They were of whitish color and less than 5 millimeters in diameter.

Microscopic examination of the thymic growth revealed a diffuse proliferation of lymphocytes, which varied in size. The supporting framework was very scanty. No Hassall's corpuscles were found. The metastatic nodules in kidneys and retroperitoneal lymph nodes and the diffuse thickening of the pericardium and pleura consisted of the same uniform overproduction of lymphocytes. The diaphragmatic pleura was covered with a thick layer of tumor cells which had also infiltrated the muscle to a marked degree.

**Anatomical diagnosis** Lymphosarcoma of the thymus involving the pericardium, pleura, and diaphragm. Metastases in kidneys and retroperitoneal lymph nodes.

**CASE 2** C. M., 41 years of age, white, male, was admitted to St. Francis Hospital June 2, 1936. For 7 weeks, he had had attacks of precordial pain without relation to effort. He had been treated for gastric ulcer, but the attacks of pain increased in length and severity. On admission to the hospital a marked swelling of the left side of the neck was noticed. Examination of the chest disclosed dullness and absence of breath sounds over the left lung. The heart sounds were faint, there were no murmurs. The pulse rate was 104 and the blood pressure 120/85. The electrocardiogram showed depression of the ST<sub>1</sub> and ST<sub>2</sub>, and an inverted T. These changes were interpreted as suggestive of coronary occlusion. The white blood cell count was 8,300 and the red blood cell count 4,500,000. The hemoglobin (Sahli) was 88 per cent. The Wassermann test was negative. The urine had a specific gravity of 1.022, chemical and microscopic examination were normal.

Roentgenological examination showed a dense cloudiness throughout the left lower half of the chest, suggesting pleural effusion. Fifty cubic centimeters of pleural fluid were obtained. The fluid was slightly bloody, the sediment had 95 per cent lymphocytes. No bacteria were found. Inoculation of the sediment into two guinea pigs did not reveal tuberculosis. Two weeks after admission, the patient became increasingly dyspneic and cyanotic. The left chest was tapped on 6 occasions and, in all, 4,500 cubic centimeters of bloody exudate were withdrawn. There was only temporary relief. From July 2 on the patient was unable to eat and sleep because of dyspnea, he became extremely restless and died July 12, 1936.

At postmortem examination it was found that the supraclavicular lymph nodes on the left side were moderately enlarged. Their cut surface was firm, grayish white. On removing the sternum, a mass was found corresponding to

## HELLWIG: MALIGNANT THYMOMA

the position and form of the thymus. It was triangular in outline with the base downward and measured 3 by 8 by 10 centimeters. It was firmly attached to the anterior surface of the pericardium encasing the heart in a 3 centimeters thick leatherlike layer. Direct extension from the growth covered the parietal pleura at the base of the left lung. The left pleural cavity contained about 400 cubic centimeters of bloody thin fluid. The lung tissue and the bronchi were not invaded. The cut surface of the thymic growth was yellowish-white, without cysts or hemorrhage. There were no secondary deposits in any part of the body. The spleen was of double size, the cut surface was very soft and of grayish-red color.

Microscopic examination of the thymic tumor revealed a cellular growth composed of closely packed lymphocytes. The framework was inconspicuous. In one section several small Hassall's corpuscles were found. In the pericardium and in the pleura covering the left lower lobe of the lung, thick layers of lymphocytes were seen.

Anatomical diagnosis: Lymphosarcoma of the thymus gland, extending to the pericardium and the left pleura.

CASE 3. J. H., 25 years of age, white, male, came to St. Francis Hospital on October 9, 1934. Four days earlier he suffered pain in the cervical region and noticed an enlargement of the neck above the clavicles. He had no difficulty in breathing and had not lost any weight. Physical examination showed a well nourished young man. His left pupil was dilated and did not react to light and accommodation. The tonsils were slightly swollen, the lips were bluish. The veins of the neck were distended. In the supraclavicular region a firm mass was found which did not move with swallowing. The thyroid was not palpable. The patient had a brassy cough. There was dullness from the upper border of the sternum to the fourth intercostal space and extending 6 centimeters lateral from both margins of the sternum. The breath sounds were almost completely absent over this area. The heart beat was outside the midclavicular line. There were no thrills or murmurs. The aortic sounds were distant. The blood pressure was 142/86.

Liver and spleen were not palpable and there were no masses in the abdomen. The axillary and inguinal lymph nodes were not enlarged. The urine was clear, the specific gravity was 1.006, the chemical tests for albumin, sugar, blood, and bile were negative. The red blood cell count was 4,700,000, the white blood cell count 8,100, hemoglobin (Sahli) was 81 per cent. The Wassermann test was negative.

Roentgenological examination disclosed a large dense mass in the upper mediastinum. On October 10, 1934, a small incision was made on the upper border of the sternum into the anterior mediastinum. It was firm, not encapsulated, but fairly circumscribed. A triangular piece, measuring 14 by 8 millimeters, was removed for microscopic study.

The tumor was composed of densely packed cells with very little stroma. The cells were of the small lymphocyte type with variation to the large lymphocyte. The nuclei were large and stained dark. Nucleoli were not seen. The cytoplasm was slight, but clearly stained. Few mitoses were found. There were no Hassall's corpuscles or cells suggesting a thymic reticulum present. Few eosinophilic cells were found. The tumor was divided into irregular lobules by vascular septa from which a reticulum ramified between the tumor cells.

Histological diagnosis: Lymphosarcoma. The patient received intensive treatment with deep x-ray radiation but had only temporary relief. The symptoms of intrathoracic pressure became more and more manifest: cyanosis, dyspnea, edema of the neck and face, cough and pain became progressively worse. The patient's gen-

eral condition became rapidly worse and he died on April 10, 1935, 6 months after radiation had been begun.

CASE 4. Mrs. T. C., a white married woman, 30 years of age, was admitted to St. Francis Hospital December 28, 1936. Two years previously she had been treated for syphilis. In February, 1935, her tonsils had been removed. Since August, 1936, she has had severe pain in the back radiating down to both arms. Associated with the pain, she had choking sensation, coughing spells, and difficulty in breathing. Swallowing of food became difficult, especially if the food was not chewed well. These complaints were worse at night. At times the patient noticed a large lump appear on the side of the neck.

Physical examination on admission showed a well nourished and well developed white female. There were masses on each side of the neck. The thyroid was not palpable. The thorax was symmetrical; there was an area of dullness, 6 centimeters wide, on each side of the sternum. The breath sounds were diminished. The abdomen was soft and flat. No masses were palpable. The basal metabolic rate was 6 per cent above normal. The red blood cell count was 3,180,000; the white blood cell count 9,150, with 61 per cent segmented leucocytes and 30 per cent lymphocytes. The urine was clear and of straw color. The chemical and microscopic findings were normal.

Roentgenological examination showed the heart shadow mostly obscured and there was a wide mediastinal shadow. A barium capsule stopped in the esophagus at the first dorsal vertebra.

A diagnosis of mediastinal tumor was made, but the patient left the hospital refusing x-ray treatment. She returned on March 23, 1937, complaining of abdominal distention. A mass could be palpated in the pelvis and a diagnosis of uterine myoma was made. On March 24, 1937, a laparotomy was performed. Both ovaries were found markedly enlarged, and a third tumor was found attached to the posterior wall of the pelvis. The 3 tumors were removed.

The pathological specimen consisted of 3 solid oval tumors, two with tubes attached. The ovarian masses measured 6.5 by 5 centimeters and 7.5 by 6 centimeters, respectively. The third specimen measured 6 by 3.5 centimeters. The three tumors had an identical, whitish, brain-like cut surface with several cystic areas.

Microscopic examination showed the tumors to be composed of closely packed lymphocytes with some variation in size. The nuclei were hyperchromatic, the nuclear material was evenly distributed, and there were no distinct nucleoli. The stroma consisted of fine strands of connective tissue. The tumor tissue was richly supplied with small capillaries. Several hemorrhagic areas were encountered. In one ovarian tumor a fresh corpus luteum was present.

Histological diagnosis: Lymphosarcoma in both ovaries and in pelvic lymph node.

After recovery from the operation, the patient received intensive courses of deep x-ray radiation of the mediastinal tumor. The symptoms of increased intrathoracic pressure became more and more alarming. A large mass developed in the right side of the chest. Hard tumors appeared in the right axilla and in the right breast. There was marked edema of the upper extremities. In October, 1937, respiration became extremely labored, cyanosis developed, and the patient had to sit up to breathe. She died October 16, 1937, 9 months after onset of her illness.

## LEUCOSARCOMATOSIS

In a series of cases a large thymoma with leucemic blood picture has been described (Fabian),

so that leucemia with involvement of the thymus has been recognized as an atypical variety. It was Sternberg who established the term "leucosarcomatosis" and sharply separated it from the ordinary type of leucemia. He believed that it represents a true tumor process. Autopsy in these cases showed, besides generalized swelling of the lymphatic apparatus, a local lymphosarcomatous growth with invasion of surrounding organs. Four of Sternberg's 6 cases of lymphoid leucosarcomatosis had large mediastinal tumors which had the microscopic structure of lymphosarcoma. They involved the pericardium, the great vessels, and lungs. The spleen was often enlarged, and the liver and kidneys showed streaks of infiltration. The primary growth may exist for weeks, months, or years before invasion of blood stream occurs, but when it does involvement is abrupt, and the process advances with astonishing rapidity.

Haagensen's case, in a 59 year old man, embodied the characteristic features of leucosarcomatosis as they have been described by Sternberg. The mediastinal tumor decreased markedly in size under radiation, but the disease was uncontrollable as a whole. Friedlaender and Foot reported a case of malignant small celled thymoma with acute lymphoid leucemia in a 38 year old colored female. Craver and MacComb observed 4 cases of lymphatic leucemia accompanied with marked enlargement of the thymus. In 1 case, light radiation of the thymic tumor caused a drop in the white blood cell count from 58,000 to 1,800. However, the patient, a 6 year old child, died 3 months later. Autopsy revealed a diffuse lymphoma of the thymus with hyperplasia of the tonsils and lymph nodes, and lymphocytic infiltration of the kidneys, spleen, lungs, heart, and liver.

Major's case, a 42 year old female, had a white blood cell count of 41,000 with 65 per cent lymphocytes. At autopsy, a mediastinal tumor, 10 by 7 by 7 centimeters, was found which was composed of lymphocytes and which contained few concentric structures resembling Hassall's corpuscles. Major did not find definite criteria as to whether the thymic tumor or the blood dyscrasia was primary. Margolis, who observed in 28 cases of lymphatic leucemia 4 with thymic tumor, is of the opinion that the tumor represents merely part of the tendency to lymphocytic infiltration of various organs in leucemia. However, Sternberg's separation of leucosarcomatosis from leucemia has been accepted by many pathologists and has served to emphasize that there are different types of lymphocytic proliferation associated with leucemia and that in some cases the process closely approaches a malignant tumor.

**CASE 5** Mrs. M. St., a white married woman, 25 years of age, entered St. Francis Hospital on September 30, 1936 about 3 weeks previously she had pain in her stomach region. She got some relief under heat application. There was no loss of appetite and no fever. Shortly afterward, the patient began to cough and had difficulty in breathing. This became progressively worse until she had to sit up in bed. On different occasions, she had bloody sputum. During the last 3 weeks she lost about 10 pounds.

On admission to the hospital the patient appeared well nourished, she had severe pain in the chest. No palpable lymph nodes were found. The thorax was symmetrical. There was an area of dullness over the mediastinum and the left lung. The heart was not enlarged. Pulse rate was 98, the blood pressure was 110/70, and the respiratory rate 20. The spleen and liver were not palpable. The urine had a specific gravity of 1.015, the chemical and microscopic findings were normal. Hemoglobin (Sahli) was 80 per cent, the red blood cell count 3,040,000, the white blood cell count 84,450. The differential count showed 7 per cent segmented leucocytes and 85 per cent lymphocytes with many lymphoblasts. The Wassermann test was negative. Deep x ray treatment was given over the mediastinum, but the patient failed rapidly, became nauseated, and was unable to eat or sleep. The area of dullness in the chest increased in size, the cyanosis and dyspnea became worse. Finally, intermittent fever developed and the patient expired October 31, 1936, less than 3 months after the onset of the disease.

At postmortem examination the anterior mediastinum was found to be completely occupied by a wedge shaped hard mass which measured 14 by 6 centimeters and extended from the suprasternal notch downward over the surface of the pericardium as far as the diaphragm. It infiltrated the pericardium and the anterior margin of both lungs. The great vessels at the base of the heart were surrounded by the growth, and the large bronchi were completely encased. There were no tumors in the lung tissue nor in the walls of the bronchi. The pleural cavities contained about 500 cubic centimeters of bloody fluid. The spleen was three times normal size, and there was a large anemic infarct on the upper pole. The pulp was soft, homogeneous, grayish red. The liver was soft, not enlarged and the color of the cut surface was light brown. Lymph node enlargement was encountered only in the mediastinum.

Macroscopic examination of the thymic tumor showed the presence of diffuse overgrowth of lymphoid cells. The cells were closely packed and the stroma was scanty. The nucleus of the tumor cells was round, dark stained, and the cytoplasm was nongranular and light stained. No Hassall's corpuscles were seen. In kidney and liver, streaks of lymphocytes were found in the interstitial tissue and the pulp of the spleen had a diffuse hyperplasia of lymphocytes and lymphoblasts. No Balthipian bodies were found.

Anatomical diagnosis: Leucosarcomatosis of the thymus. Invasion of the pericardium and both pleural surfaces. Splenomegaly. Lymphocytic infiltration of liver and kidneys.

#### HODGKIN'S DISEASE

Hodgkin's disease of the mediastinum is a well identified local form of this disease. At autopsy it is often difficult to state whether the process arises in the lymph nodes or in the thymus since at the time when death occurs, Hassall's corpuscles are, as a rule, no longer found. Ziegler reported 3 cases of this type. The process forms a massive tumor which infiltrates the pleura and the peri-

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cardium, and surrounds and compresses the blood vessels, the trachea, and bronchi. There is often involvement of the bronchial and cervical lymph nodes and of the lung tissue. Ewing who, in 1916, reported 3 such cases, regards this type of thymoma as a form of infectious granuloma arising from the epithelial reticulum of the thymus, with many lymphocytes persisting. He found giant cells which were different from those of Hodgkin's disease in other parts of the body. They were very large, the cytoplasm was acidophilic, and the nuclei were hyperchromatic. Ewing separated Hodgkin's disease of the thymus from other forms

Fig. 1. Case 1. Thymic lymphosarcoma.

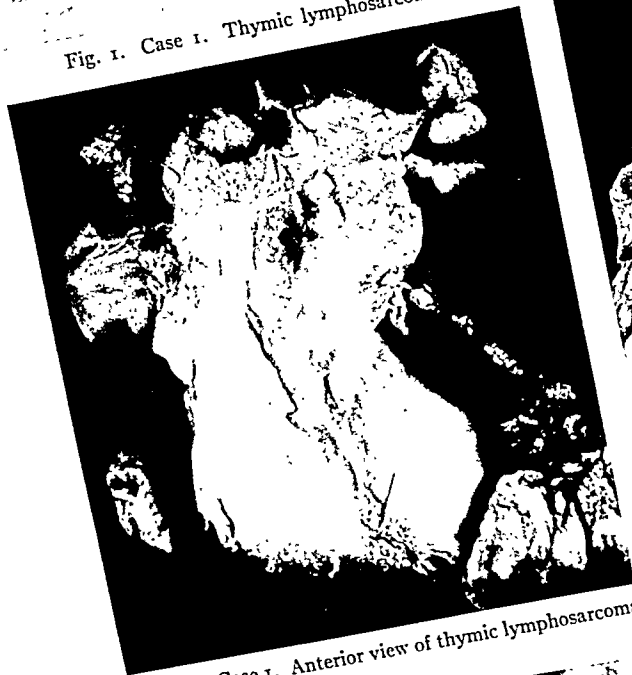


Fig. 2. Case 1. Anterior view of thymic lymphosarcoma involving pericardium.



Fig. 3. Case 1. Posterior view of thymic lymphosarcoma compressing large vessels and bronchi.

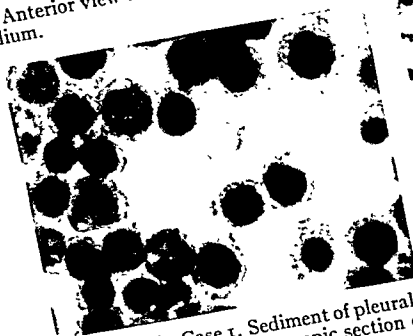


Fig. 4, left. Case 1. Sediment of pleural fluid, showing lymphocytes and lymphoblasts.

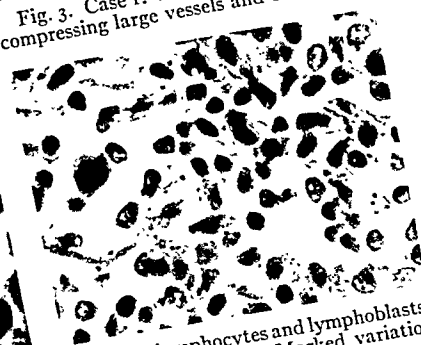


Fig. 5. Case 1. Microscopic section of thymic lymphosarcoma. Marked variation in size and form of cells.



Fig. 6 Case 2 Roentgenogram of thymic lymphosarcoma.



Fig. 7 Case 2 Anterior view of thymic lymphosarcoma, extending to pericardium and left pleura

of Hodgkin's disease and attributed its malignancy to its origin from the peculiar reticulum cells of the thymus.

A thymic origin has been most apparent in the observation by Wollstein and McLean in a 4½ months old infant. The thymus was enlarged but free and encapsulated. It showed the typical structure of Hodgkin's disease. The organs immediately surrounding the thymus were not involved, but many abdominal and some thoracic nodes as well as the spleen, liver, and kidneys were infiltrated. Simmons and Benet reported the results of radiation in mediastinal Hodgkin's disease. Although none of their patients was cured, 1 survived for 5 years. Desjardins observed a case with mediastinal Hodgkin's disease in which the tumor had been kept under control 3½ years.

Haagensen's first case of mediastinal Hodgkin's disease, in a 27 year old male, improved markedly under x-ray treatment. He died 4 years after the onset of the illness. At autopsy no trace of the large mediastinal mass was found which roentgenographic studies proved to have existed 3 years previously. In his second case, a 22 year old female, the mediastinal process regressed only partially and very slowly under adequate doses of radiation. The patient died 2 years after the tumor was noticed.

Andrus and Heuer observed a case of thymic Hodgkin's disease in a 15 year old boy. The diagnosis was established by biopsy. Sixteen months after radiation there was no appreciable change in the size of the mediastinal shadow although the density appeared slightly decreased.

In the 5 cases of Hodgkin's disease of the thymus reported by Symmers the patients died from 12 weeks to 3 years after the onset of pressure symptoms. Two of his cases had x-ray treatment without apparent results.

CASE 6 H S., 21 years of age, white, male, was admitted to St. Francis Hospital on July 8, 1938. He had not felt well for the last 9 weeks and had to stay in bed part of the time. He had had chills and fever, had been coughing considerably, and had lost about 30 pounds in weight. On admission to the hospital, his temperature was 104 degrees, his pulse, 134, respiratory rate, 30. His tongue was cherry red with irregular white patches. The glands of the neck were slightly enlarged. The chest expansion was equal, there were coarse rales and increased fremitus over both lungs. The clinical impression was that the patient had an infectious disease. Laboratory tests for malaria, typhoid fever, tuberculosis, and tularemia were negative. The examination of the urine did not show abnormal findings. In the stool were many red blood cells but no parasites were found. The hemoglobin was 8.4 grams, red blood cell count, 2,720,000, white blood cell count, 4,500. There were 2 per cent eosinophilic cells, 3 young forms, 21 band forms, 35 segmented, 37 lymphocytes and 2 monocytes. Kline flocculation test was negative. Roentgenological examination of the chest revealed the pleural angles clear, the heart not enlarged. There was no consolidation of the lungs. The upper mediastinum was wide and dense and the markings of the lung hilus were increased. X-ray study of the colon after barium enema, showed normal filling and normal motility. On July 13, the spleen became palpable 4 centimeters below the costal margin. A clinical diagnosis of Blunt's disease was made, and on July 29, laparotomy was performed. The spleen was found to be markedly enlarged. The attempt to remove it was unsuccessful on account of hemorrhage from the friable splenic tissue. The patient expired the following day, 22 weeks after the first symptoms had been noticed.

At postmortem examination it was found that the upper mediastinal region was occupied by a firm whitish tumor which imitated the two lobes of the thymus. The left lobe measured 6 by 3 centimeters and the right 4 by 2 centimeters. The tumor was adherent to the surrounding structures. The peribronchial lymph nodes were enlarged and infiltrated with tumor tissue. No nodules were found in the lungs. The cut surface of the thymic tumor was grayish

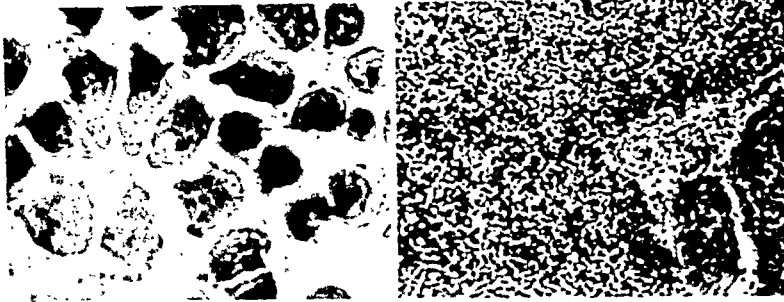


Fig. 8. left. Case 2. Sediment of pleural fluid, consisting of polygonal and round lymphoid cells.

Fig. 9. Case 2. Microscopic section of thymic lympho- sarcoma.

white, there were irregular brown and hemorrhagic areas. The heart was small and not involved in the tumor process. The cervical lymph nodes were moderately enlarged and of firm consistency. The spleen weighed more than 500 grams and the capsule was ruptured at the lateral margin. There was a large hematoma surrounding the spleen. The cut surface of the spleen was purplish-red, and there were many whitish nodules, from 1 to 3 centimeters in diameter, protruding over the cut surface. The mesenteric glands were of normal size, but the retroperitoneal lymph nodes were markedly enlarged and had a firm grayish-white cut surface.

Microscopic examination showed the thymic tumor to be composed of a diffuse proliferation of reticulum cells, lymphocytes, and giant cells of the Sternberg-Reed type. Necrosis and fibrosis were present in many sections. Eosinophilic cells were scanty in the mediastinal growth, but abundant in the bone marrow of ribs and vertebrae which were infiltrated with typical Hodgkin's tissue. The nodules in the spleen and in the retroperitoneal lymph nodes also

had the histological structure of Hodgkin's disease. In the periportal tissue of the liver few areas of cellular proliferation were found. The most important cell types in all these lesions were large rounded cells with clear protoplasm and single or multilobed hyperchromatic nuclei.

CASE 7. Mrs. J. H. R., a middle aged white woman, complained on August 10, 1937, of an itching eczema below the right nipple. It formed a scale and when peeled off, left a raw, pink colored area, about 1 centimeter in diameter. This lesion recurred time and time again and resulted in discoloration and thickening of the skin. Three physicians saw this patient and made a tentative diagnosis of Paget's disease. Dr. E. E. Talley, on December 10, 1938, removed a piece of skin for examination. Microscopic examination showed proliferation of the epidermis with elongation of rete pegs. The cells were well differentiated and did not show the characteristics of Paget's disease. The corium was densely infiltrated with round cells which had the appearance of lymphocytes and plasma cells. No eosinophilic cells or Sternberg-Reed cells were found. The microscopic diagnosis was: chronic dermatitis. After this biopsy, the patient felt very well. She gained in weight up to 211 pounds by December, 1939. When her physician saw her again in September, 1940, her weight had decreased to 175 pounds, and she was very weak, tired easily, and her skin was pale. Hemoglobin was 65 per cent, the red blood cell count 3,450,000. Roentgenological examination of the chest revealed a large mass in the upper mediastinum extending 7 to 8 centimeters to both sides from the sternum. The mass was not pulsating. The heart was slightly enlarged. The Wassermann test was negative. The only symptoms of increased intrathoracic pressure were cough and some pain in the left shoulder. On the patient's hands and arms, and on the back of her neck, indurated, raised, pink areas appeared



Fig. 10. Case 3. Roentgenogram of thymic lymphosarcoma.

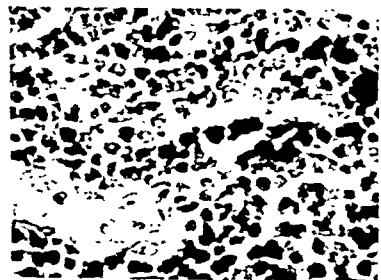


Fig. 11. Case 3. Microscopic section of biopsy specimen.



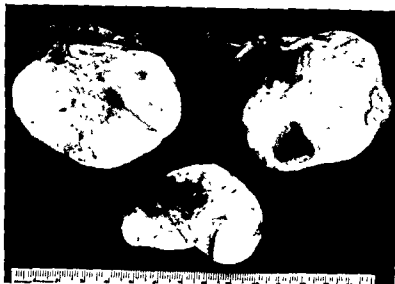


Fig 12 Case 4 Metastases of thymic lymphosarcoma in both ovaries and in pelvic lymph node.

about 0.5 to 1 centimeter in diameter. There was no itching. These areas were similar in appearance to the skin lesion near the nipple removed in 1938. On December 11, 1940, her physician removed a hard lymph node from the neck. It measured 2 by 1.2 centimeters and had on cross section a homogeneous whitish appearance. Microscopic examination showed complete obliteration of the normal structure of the lymph node. There was a diffuse growth of lymphocytes and polygonal, pale reticulum cells. These large cells had a vesicular nucleus and a tendency to form a syncytium. Several giant cells with one or several dark stained nuclei were present and few eosinophilic cells were encountered. There was no evidence of necrosis or fibrosis in the lymph node.

**Histological diagnosis** Hodgkin's disease.

From the clinical, roentgenological and histological findings the case was interpreted as thymic Hodgkin's disease with manifestations of the disease in skin and cervical lymph nodes.

#### CARCINOMA

Carcinoma is the rarest form of malignant thymoma. It originates from the epithelial reticulum

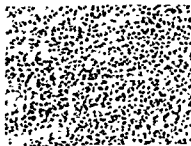


Fig 13. Case 4 Microscopic section of ovarian tumor

of the thymus and consists of sheets and strands of epithelial cells lying in a dense connective tissue stroma. The tumor cells tend to be flat, vary in size and shape, and may form concentric whorls resembling Hassall's corpuscles, not only in the primary growth, but also in metastases.

The best examples of this type have been reported by Symmers and Vance, Jacobson, Foot, Margolis, Obiditsch, and Brannan. More common are the forms of thymic carcinoma which are made up of two types of cells, flat epithelial cells



Fig 14 Case 4 Roentgenogram of primary lymphosarcoma in thymus



Fig. 15. Case 5. Leucosarcomatosis of thymus, involving pericardium and both pleural surfaces.

originating from the thymic reticulum, and lymphoid cells which are derived from the small thymic cells. The structure of these tumors is identical with that of the lympho-epitheliomas which occur in or around the pharynx. Matras and Priesel discussed this form of malignant thymoma and reported 7 cases of their own. The same type was described by Rubaschow, Largiadér, and Schmidtman.

In 1932, Crosby collected from the literature

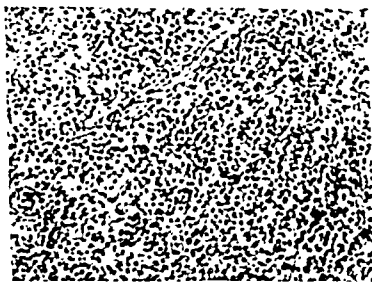


Fig. 16. Case 5. Microscopic section of thymic leucosarcomatosis.



Fig. 17. Case 6. Anterior view of Hodgkin's disease of the thymus.

36 cases of thymic carcinoma with autopsy reports. As regards sex, 25 occurred in males and 10 in females. In one case report the sex was not stated. The majority of cases occurred after the age of forty. The oldest patient was 72 years old, while in 1 case the tumor was found at birth. The tissues in close proximity to the thymus were almost always invaded. In 3 of the cases of thymic carcinoma no metastases were found. While uncommon below the diaphragm, meta-

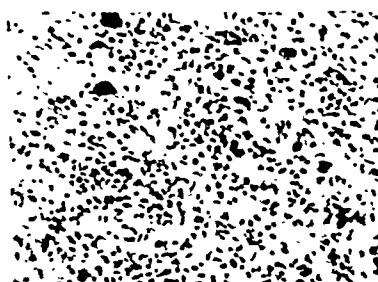


Fig. 18. Case 6. Microscopic structure of thymic Hodgkin's disease. Sternberg-Reed cells are numerous.



Fig 19 Case 7 Roentgenogram of Hodgkin's disease of the thymus

stases may take place to almost any organ of the body.

The information concerning the reaction of thymic carcinoma to radiation is meager. In the case reported by Foot, weekly irradiation with deep x-ray had no apparent effect on the tumor. Lenk described an epithelioma of the thymus, proved by autopsy, which showed no change following intensive radiation. Haagensen's 2 cases of anaplastic carcinoma of the thymus were definitely radioresistant. Although heavily irradiated they decreased but slightly in size, and death occurred in short time. Cutler reported a case of thymic carcinoma in a 56 year old man who in spite of two courses of high voltage roentgen therapy did not show any improvement.

In a number of cases, operative removal of thymic carcinoma has been attempted (Margolis), without success.

CASE 8 Mrs P S, a white married woman, 23 years of age, entered St Francis Hospital on September 26, 1939. Three weeks previously the patient had cough, dyspnea, and pain in the chest radiating to the left axilla and left side of the neck. She had some fever and became anemic. There was enlargement of lymph nodes in the left cervical

region and in the left axilla. Her white blood cell count was 10,000, without changes in the differential count. The pulse was 120, the temperature 37 degrees, and the pulse rate 26. A lymph node was removed for examination from the left side of the neck. It measured 2 by 1.6 centimeters, was hard, and had a grayish cut surface. Microscopic examination revealed a peculiar structure, difficult to interpret. While some areas resembled Hodgkin's disease, others were more in favor of a diagnosis of carcinoma. There were sheets and cords of large flat or polyhedral cells lying in dense connective tissue. Several concentric layers of cells were found which formed wheel like structures resembling Hassall's corpuscles. Lymphocytes, plasma cells, and eosinophilic cells were irregularly distributed. Many giant cells were found with opaque acidophilic cytoplasm and dark, vesicular nucleus.

Röntgenological examination of the chest revealed a large area of increased density in the mediastinal region extending to the left. Its central portion was very dense, at the left there were mottled areas of lesser density. The shadow was broadest at the level of the left fourth inter space. Its edges were irregular.

Deep x ray treatment was given to the mediastinal tumor, and there was evidence of improvement. The patient returned home and soon marked exacerbation of symptoms occurred. There was increased dyspnea, cough and pain. The superficial veins of the chest became engorged, edema of the face and of the left arm developed. The area of mediastinal dullness widened; signs of fluid showed in both pleural cavities. Her general condition grew rapidly worse, she died April 23, 1940, 8 months after first symptoms.

At postmortem examination it was disclosed that the right diaphragm was in the level of the sixth, and the left in the seventh intercostal space. Both pleural cavities contained about 2,000 cubic centimeters of clear amber fluid. There were 150 cubic centimeters of light brown fluid in the pericardial sac. When the sternum was removed, a large hard mass was found to extend from the suprasternal notch to the upper half of the pericardium. The tumor had the form of the thymus gland, was 12 centimeters wide and weighed 850 grams. Trachea, esophagus, and the right and left bronchus were firmly surrounded by the tumor. The great blood vessels at the base of the heart and thoracic arches were compressed by the extension of the growth into the pericardium. Several small hard nodules, 1 to 2 centimeters in diameter, were found at the surface of the right and left upper lobe of the lungs. The lung tissue itself was not invaded. Cross section of the thymic tumor revealed a hard, whitish tissue with small yellowish areas.

In the peritoneal cavity 1,500 cubic centimeters of amber fluid was found. The peritoneum was glistening and without tumor nodules. Liver, kidneys, adrenals, and pelvic organs were free from tumor. The spleen weighed 170



Fig 20, left Case 7 Giant cell

Fig 21 Characteristic structure of lymph node in case of thymic Hodgkin's disease

4. Differential diagnosis between malignant thymoma and benign mediastinal tumors is imperative, since successful removal of the latter has been recorded. The differential diagnosis of the various pathological types of thymic tumor is of practical value because some can be temporarily controlled by radiation.

5. There is no clinical or roentgenological sign to differentiate accurately between the different types of malignant thymoma. Exact diagnosis depends on microscopic study of tumor tissue which may be accessible to biopsy.

6. While thymomas originating from lymphoid tissue are more radiosensitive than thymic carcinoma, at the present no cure has been obtained in either group.

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# COMMON BILE DUCT PERISTALSIS

## Preliminary Report

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**A** SEARCH of the literature reveals that there is no record of common duct peristalsis having been observed in man. The present report has to do with such an observation. This was clearly visualized under the fluoroscope as an accidental finding, while a study was being made of a pathological common duct, and it was immediately recorded by pictures. This finding is of more than academic interest. Explanations and descriptions accompany the figures.

This study will be continued as soon as conditions permit. The present case is reported because war conditions are such that thorough and complete investigation cannot now be carried out.

The accompanying pictures show clearly and conclusively that there are changes in the internal diameter of the common bile duct. What are the possible causes? They are (1) changes in intra-abdominal pressure; (2) changes in pressure or position of organs lying alongside; (3) changes in pressure from without (through tube), (4) drugs (amyl nitrite), (5) irritation by the T tube, (6) sphincter of Oddi tissue extending into the duct, and (7) actual peristalsis. Because the location of the changes is in the distal end of the duct, which is retroperitoneal, the first two are not likely. The tube was clamped, and drugs were not used. Hence



Fig 1

Fig 1 Cholangiogram made 10 minutes after  $\frac{1}{2}$  grain of morphine had been given, and approximately 3 minutes after the injection of 15 cubic centimeters of lipidol. In this figure the dye is observed just beginning to enter the duodenum. The interpretation of this picture by itself would indicate either a ductal or pancreatic pathological condition. This entire narrow channel is not a single constriction. It is longer than the areas seen by fluoroscope.



Fig 2

If it is all constriction it is not the same as intestinal peristalsis, but, judging from the subsequent pictures, only the upper part is involved.

Fig 2 Cholangiogram made 2 minutes after Figure 1, and 5 minutes after the injection of the dye. More dye has entered the duodenum. The outline indicates that the distal end of the duct has completely closed. The hepatic ducts are well filled.



Fig. 3

Fig. 3. Approximately 5 minutes later. The distal end of the duct is open and the contrast medium is flowing freely into the duodenum. The hepatic ducts are almost empty compared with Figure 2, because this area is the source of the enlarged duodenal content.

Fig. 4. The duct is now closing. The T-tube is almost empty. All pictures show a point of leakage at the entrance of the tube into the duct. This had disappeared the next



Fig. 4

day; it probably drained through the sinus. Notice that the dye is flowing cephalad. This is a good example of reverse duodenal peristalsis which Ivy believes is a cause of biliary stasis. It is not uncommon to see the dye, during serial cholangiograms or by fluoroscope, first traveling in an antiperistaltic direction, then changing to normal. On one occasion the dye did actually enter the pyloric antrum.

the only three possibilities are irritation by the tube (foreign body); contraction of sphincter muscle, and active peristalsis. Irritation could not produce such changes unless the inherent ability to contract and relax was present; the sphincter muscle is affected by morphine and this must therefore be considered, but it is unusual for sphincter tissue to extend so far up the duct—unless the duct passes through the duodenal wall for an abnormally long distance. It is therefore concluded that in this particular patient the common bile duct has the ability to move its contents onward by active effort. The writer has no doubt about this, because the fluoroscopic study showed distinctly and clearly that the shadow of the dye was changed in shape by a temporary constriction, and that a segment of lipiodol distal to the con-

striction was rushed forward into the duodenum. It was because of this that serial pictures were taken. The areas of constriction, as seen under the fluoroscope, were not "caught" in the pictures. This was not due to "milking" by the duodenum, because the constriction was one inch away from the end of the duct as determined by the shadow in the picture.

Peristalsis is activated and excessive proximal to any obstruction in a hollow tube. In this instance a partial obstruction is artificially produced by morphine. *But*, peristalsis cannot be activated unless it is present in either an active or a latent form.

Should we expect to find peristalsis in the common duct? I think so. Why? Because this duct is an integral part of one of the most important

physiological functions of the body and an uninterrupted onward flow of bile is essential to good health. There must be some mechanism, other than just back pressure, to overcome transient states of obstruction. I do not believe that the common bile duct is an inactive, inert, impassive, and immobile hollow tube. This case report indicates that such is not the case.

One of many clinical applications of this finding is that serial cholangiographs should be taken, because the interpretations of single and serial plates

will differ. The latter will, of course, be more correct; the single plate may be misleading. (See Figs 1 to 4).

#### SUMMARY

A singular observation, never before observed, is recorded because it *indicates* that the common duct of man has the inherent ability to propel its contents forward. The mechanism of this peristalsis is not discussed. A more extensive report will follow.

## ACROMIOCLAVICULAR SEPARATION

### New Method of Repair

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**A** CROMIOCLAVICULAR separation may be a seriously disabling injury, due to coincidental tearing of the coracoclavicular ligament. This ligament may be likened to a stout cord by which the scapula, and with it the whole upper extremity, is suspended from the outer end of the clavicle. If this cord be ruptured, the arm drops helplessly to the side and the tip of the clavicle projects upward, tenting the skin over it.

Anatomically, the acromioclavicular articulation is a weak spot at a point of great stress (Fig. 1). Upon it are focused the antagonistic actions of powerful muscle groups, plus the weight of the upper extremity and the added strain of lifting and pulling. The joint surfaces are small, flattened, and obliquely placed, that of the clavicle facing downward and backward. A joint cartilage may or may not be present. The capsular ligaments are not strong and the joint would be dislocated far more frequently were it not for the coracoclavicular ligament. This structure has two groups of short tough fibers, the conoid and trapezoid ligaments, so placed as to reinforce the joint no matter in what direction it moves.

Motion in this joint may be of almost any type but is always very slight, being checked by the coracoclavicular ligament. As Codman has pointed out, "Nature made it slightly movable in order that it might: (1) swing a little . . . (2) rock a little . . . (3) twist a little . . . (4) slide a little inward . . . (5) act like a hinge." Although perfect shoulder motion requires a movable acromio-

clavicular articulation, fusion of the joint will not embarrass ordinary shoulder function. As a matter of fact, during unrestricted motion of the upper extremity in all directions the acromion moves to such a slight extent upon the clavicle that, in a recent fluoroscopic study of several thousand shoulders, I was never able to detect the exact extent of acromioclavicular motion (1).

Injury usually results from a direct blow upon the acromion, as from a fall. Treatment aims at re-establishment of the integrity of the coracoclavicular ligament or substituting therefor some other means of support between scapula and clavicle. Various slings, harnesses, and dressings have been devised to support the arm and depress the outer end of the clavicle. They all necessitate severe restriction of shoulder joint motion for a considerable period of time and, in cases of complete disruption, fail to re-establish adequate support (Fig. 7a).

Numerous operative procedures have been recommended. Perhaps the one most commonly employed has been that of looping a strip of autogenous fascia under the coracoid process and over or through the clavicle. This is a major operative procedure which requires a general anesthesia, two separate good sized incisions, and a prolonged hospitalization. Even in experienced hands it is a technically difficult operation, involving considerable trauma and attended by definite risks. In optimal cases, recovery is slow and rehabilitation prolonged. Other materials, such as silk and wire, have been used instead of fascia but have

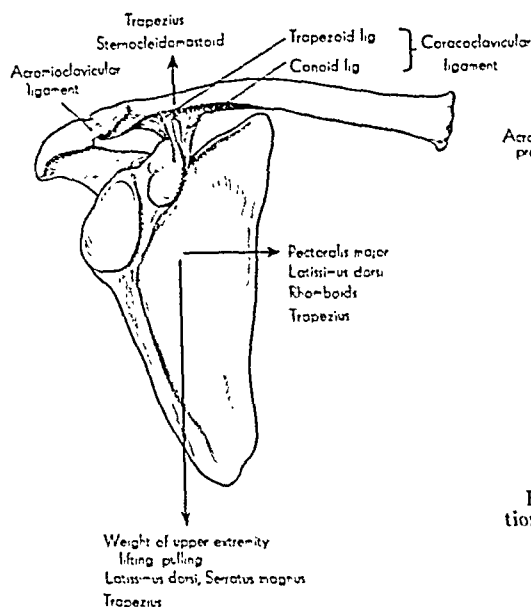


Fig. 1. Forces acting upon the acromioclavicular joint.

been unsatisfactory as they tend to cut through the bone. Frozen shoulder is not an uncommon complication.

Recently there has been reported (3) successful fixation of scapula to clavicle by passing Kirschner wires horizontally through the acromion into the clavicle. These are allowed to protrude through the skin and are removed when healing of the ligaments is thought to have taken place. Certain objections may be raised to this procedure. It is not a simple matter to insert flexible wires accu-

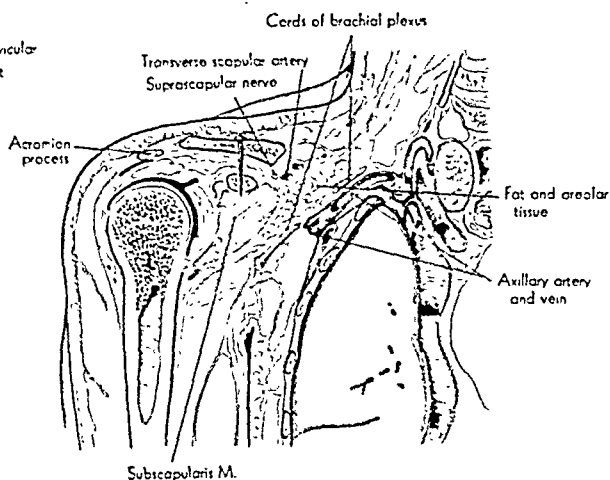


Fig. 3. Coronal section through head of humerus to show relation of screw to important structures.

ately through the acromion and clavicle in the plane of their thinnest dimensions. To give adequate support, more than one wire must be inserted. The wires may work loose due to bone absorption and active motion. Protrusion of the wires through the skin for several weeks entails a certain risk of infection. Theoretically at least, passage of even small gauge wires through the acromioclavicular joint would predispose to a localized arthritis of this joint. Finally, the wires must subsequently be withdrawn and full reliance for support be placed upon scar formation between the torn ends of the ruptured ligaments.

So far as is known, the method about to be described has never before been used. It consists

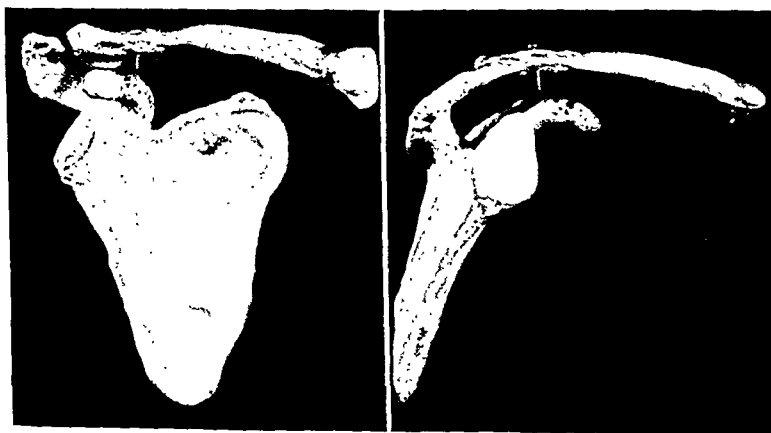


Fig. 2. Author's method of suspending scapula from clavicle by single vitallium screw.

STATE OF ARIZONA





Fig 4. P. B., aged 74 years, housewife a, Roentgenogram taken before operation b, After reduction with

screw c, 4 months after operation Note new bone forming about screw

of suspending the scapula from the clavicle by a single vitallium screw, passed through the clavicle into the coracoid, through a small incision under local anesthesia (Fig. 2).

With the patient seated upright in a chair, the acromioclavicular articulation is infiltrated with 1 per cent novocain. Infiltration is continued, to include the tissues overlying the outer 2 or 3 inches of the clavicle. A  $\frac{3}{4}$  inch incision is then made through the skin, subcutaneous tissues, and periosteum, parallel to and over the outer portion of the clavicle, about  $1\frac{1}{2}$  inches proximal to its outer end. This point is marked, upon fluoroscopic examination prior to operation, as the site at which the clavicle directly overlies the coracoid process.

A  $\frac{3}{16}$  inch hole is then drilled downward through the upper cortex of the clavicle and, after the injection of novocain, through the lower cortex.

More novocain is infiltrated through this hole into the underlying torn fibers of the coracoclavicular ligament and also into the periosteum at the base of the coracoid process of the scapula. At this stage of the procedure reduction of the dislocation should be secured and maintained by an assistant who supports the arm and depresses the tip of the clavicle. The upper cortex of the coracoid process can now be outlined rather well with the point of the infiltrating needle, and its position can be checked with a portable fluoroscope previously set up. A hole is then started with a sharp pointed awl in the upper cortex of the coracoid process, after which a vitallium screw of proper length is inserted through the clavicle into the coracoid process. As the coracoid is relatively soft bone with a thin cortex, the screw easily cuts its own way through the bone without the necessity of previous drilling.



Fig 5. M. B. aged 71 years housewife a, left Before operation b, After reduction with screw



Fig. 6a

Fig. 6b

Fig. 6c

Fig. 6. J. M., aged 65 years, laborer. a, Right shoulder before operation. b, Normal left shoulder. c, Reduction apparently complete. d, Roentgenogram from a different angle shows reduction is actually partial, although clinically satisfactory.



Fig. 6d

The hole in the clavicle is purposely made a bit larger than the screw so as to allow free play of the screw within the clavicle. In this way the scapula can be suspended without fixing it rigidly to the clavicle, and a certain degree of motion in all directions can be preserved in the acromioclavicular joint. It is important that reduction of the acromioclavicular separation be maintained until the screw is actually in position. Failure to observe this precaution may result in a misplaced screw or pulling of the screw. Care must also be taken to have the screw penetrate both cortices of the coracoid process, to provide a strong grip on that bone.

Fortunately, no important structures are endangered by this operation (Fig. 3). The axillary vessels and the cords of the brachial plexus lie in an anterior plane deeply medial to the base of the coracoid process when the arm is at the side and are separated from the anterior surface of the subscapularis muscle by a considerable amount of fatty and areolar tissue. As the arm is elevated in the coronal plane, the vessels and nerves tend to approach the tip of the coracoid but are held for-

ward from its base by the intervening subscapularis muscle and tendon. The transverse scapular vessels and the suprascapular nerve pass medial to the base of the coracoid process and so are well out of harm's way. The cephalic vein and deltoid artery lie in an anterior and superficial plane. If the screw, when properly placed, should project through the undersurface of the coracoid process near its base, it will merely bury itself in the fibers of the subscapularis. This has been proved by repeated experiments on the cadaver, in which the screw has been introduced blindly and its position checked by subsequent dissection.

No hemostasis is required and the wound is simply closed with 2 or 3 skin clips or sutures. The operation should be performed in a hospital where adequate facilities and assistance are available, but the patient need not be admitted to the hospital and may be allowed to go home soon after the operation is completed. No sling or other support is necessary; in my opinion, it is contraindicated. Active use of the hand and arm is desired and should be encouraged from the start, but the patient must be warned against lifting or pulling



Fig 7 A M, aged 34 years, masseuse a, left, Preoperative roentgenogram shows failure of pressure dressing to maintain reduction b, Screw reduction successful

for at least 8 weeks. If the shoulder should ache or the arm become tired, prompt relief may be secured by resting the elbow on a pillow for a few moments. Frequent gentle exercises are prescribed, to be performed within pain limits. The most useful of these are the arm swinging exercise of Codman and "crawling up the wall." No passive exercises or manipulation should be done. Physiotherapy, consisting of baking or diathermy, may be employed if desired but it is not essential.

The screw is left in place indefinitely unless some indication arises for its removal. A brief report of 4 cases in which this method has been employed follows

#### CASE REPORTS

**CASE 1:** P B, aged 74 years, slipped on the stairs, grasped the rail with her left hand to save herself and fell to the floor, striking on the point of her right shoulder. She

experienced immediate severe pain in the right shoulder and total loss of use of the right upper extremity. Pain in the shoulder and inability to get in a comfortable position in bed precluded sleep that night. When first seen on the following day, the patient carried the right arm close to her side, with the flexed forearm supported by her left hand. She was in obvious pain and this was greatly aggravated by the slightest motion of the right shoulder. The outer end of the right clavicle projected well above the level of the acromion process of the scapula and there were acute tenderness and preternatural mobility of the acromioclavicular articulation. Diagnosis of acromioclavicular separation was confirmed by fluoroscopic and roentgen examination (Fig 4). A sling was fitted and mild analgesics prescribed.

This case was complicated by the presence of advanced hypertrophic osteoarthritis, most marked in the joints of the right hand and wrist, and by the fact that the patient was still convalescing from the effects of a right Colles fracture sustained only  $2\frac{1}{2}$  months prior to the present injury. Since the severe shoulder pain persisted in spite of the sling and the arthritis rapidly became worse because of it, it was felt that some form of internal support which would at once relieve the pain and free the upper extremity for motion within a reasonable range was demanded. Accordingly, 4 days after injury repair was effected in the manner described. Within 2 weeks of operation the patient was able to feed and dress herself entirely without assistance. From the time of operation there was complete relief from acute pain, the only complaints were of a heaviness in the shoulder and a slight ache when the arm became overtired from too much use. These minor symptoms disappeared after the first 10 days. The arthritis in hand and wrist immediately improved.

Two months after operation this patient fell downstairs again, this time without serious injury. Check up roentgenograms showed that the screw was pulled about  $\frac{3}{8}$  inch. New bone formation was visible along the sides of the screw and over its head. Function was not impaired and no pain was experienced. At 4 months this patient still has normal use of her shoulder without symptoms. Roentgenograms (Fig 4) show an increase in bone formation about the screw.

**CASE 2:** M B, aged 73 years, fell from a chair and sustained a complete left acromioclavicular separation with disruption of the coracoclavicular ligament (Fig 5). Operation was performed in the manner described the evening of the day of injury and the patient went home the next morning. No sling or support of any kind was worn and

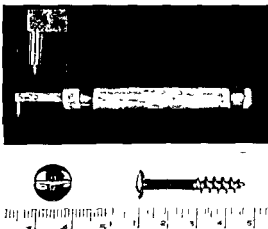


Fig 8 a, above, Clavicle depressor b, New vitallium coracoclavicular screw

the patient was instructed to use the arm as much as possible, within reason. The severe pain was immediately and completely relieved by the operation. At 10 days this patient did up her own hair and dressed herself, even to hat and overcoat, without assistance.

At 3 weeks, while doing heavy lifting, the patient pulled the screw and partial redislocation resulted. At a subsequent operation the screw was replaced. Satisfactory, although not complete, reduction was secured. It is now 7 weeks since the original operation. Position of the bones has been maintained by the screw and she is regaining shoulder function but it is still too early to give a final result in this case.

CASE 3. J. M., aged 65 years, a heavy muscled laborer, was seen in consultation 3 days after a fall which resulted in a complete right acromioclavicular separation. A well applied Velpau dressing, worn during this interval, had failed to maintain reduction of the dislocation. At operation great difficulty was encountered in replacing the clavicle in its proper relation to the acromion. It was secured with a vitallium screw in a partially reduced position (Fig. 6). Again, no sling or support was worn. He was able to feed and dress himself the day following operation. Within 1 week he had recovered full motion of the arm in all directions. This he has maintained up to the present (6 weeks) but he has not yet been allowed to do any heavy work.

CASE 4. A. M., aged 34 years, a masseuse, fell from a stool and suffered a complete left acromioclavicular separation. Following failure of a pressure dressing to maintain reduction (Fig. 7a), repair was effected with a vitallium screw (Fig. 7b), 2 days after injury. Complete active motion of the arm in all directions was possible immediately at the conclusion of the operation. As a matter of fact her motion was so vigorous that she bent the screw slightly. When seen in the office next day the patient took off and put on her hat, overcoat, and sweater without aid and with no pain or limitation of motion. It is now 5 weeks since her operation. Perfect reduction and function have been maintained but she will not be permitted to resume heavy work for another 2 or 3 weeks.

As a result of the difficulty experienced in Case 3 in reducing the dislocated clavicle and maintaining it in its proper relation to the acromion while the holes were drilled and the screw inserted, I have devised a clavicle depressor (Fig. 8a). With this instrument the tip of the clavicle can easily be moved downward, forward, and medially and held in position by an assistant without his hands encroaching upon the operative field.

While the screw used in these cases has been successful, it is not ideal in that its head is too small, its thread too fine and closely spaced, and its shaft too thin. A special screw with a broader head, a flanged thread, and a slightly heavier shaft has therefore been designed and is now available (Fig. 8b). This provides a better bearing surface on the clavicle as well as a much stronger grip in the coracoid. The head of this screw is not only slotted for the ordinary screw driver but is

recessed for use with the patented Phillips screw driver which will not slip out. The screw head is slightly beveled and has a diameter of  $\frac{7}{16}$  inch. Although the flanged threads of this new screw have a maximum diameter of  $\frac{1}{4}$  inch, the screw can easily be inserted through a  $\frac{3}{16}$  inch hole in the clavicle due to wide spacing of the threads. The shaft is  $\frac{5}{32}$  of an inch thick and  $1\frac{1}{2}$  inches in length. These measurements were decided upon as the result of careful experimental work on the cadaver.

It is surprising how active and ambitious all these patients have been immediately following the repair. It is difficult to make them realize that they have sustained a serious injury and that they must wait 6 to 8 weeks for scar tissue to reinforce the screw before they attempt any strenuous activity. Since the screw was pulled in Case 2, necessitating a second operation, I have advised against lifting or pulling for at least 6 weeks after operation. This precaution should be observed, I believe, even when the new screw with flanged threads is used, to prevent the threads from pulling through the bone. While the screw itself has been thoroughly tested in the laboratory and found to have a tensile strength of well over 300 pounds upon direct pull, it must be remembered that support really depends upon the strength of the cortical bone until such time as that is reinforced by healing of the ligaments.

#### SUMMARY

A new method is presented for the repair of acromioclavicular separation, when there is a disruption of the coracoclavicular ligament. This consists of suspending the scapula from the clavicle by a single vitallium screw inserted under local anesthesia, an operation which does not require the patient to be hospitalized. Pain is immediately relieved and function quickly restored since no immobilization or support of the arm is required. This procedure is simple, safe, inexpensive, and immediately effective. Since it is a relatively minor operation, morbidity and mortality are practically eliminated, even in elderly patients, and convalescence is greatly shortened.

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## A TEST FOR MEDIAN NERVE FUNCTION

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**L**ESIONS of the median nerve are comparatively common. According to various statistics, during the first World War they ranked next to, or even surpassed, in frequency those of the radial or radial and ulnar nerves. Among the lesions of the median nerve, those affecting the nerve at the wrist or in the palm of the hand are especially common. Here the median nerve is affected most often directly by incisions from contact with broken glass or from suicidal attempts, by falls upon the hand, by fractures of the lower end of the radius, and the like. Also the professional handling of tools that exert pressure on the palm or upon the wrist may affect the median nerve. Lesions of the median nerve located higher up are easy to diagnose since here the flexors of the fingers and of the hand are involved and the vasomotor trophic changes are sometimes very marked. If the nerve is damaged at the wrist, the motor changes affect only the  $2\frac{1}{2}$  muscles of the thenar eminence supplied by the median nerve. As the neurological picture may be confused by tendon injuries, the diagnosis of median nerve lesions at the wrist and recognition of their course are at times difficult.

In this article a simple test for median nerve palsy will be described that is equally applicable to median nerve lesions at the wrist and to those higher up, but it is more appropriate for the diagnosis of the former. The only reference to this test I was able to find in the literature is that in the work of Pitres and Testut.<sup>1</sup> The test is so self-evident and simple that it may also have been described elsewhere; yet it is so useful that it deserves detailed description and renewed emphasis.

If the median nerve is damaged at the wrist, the muscles affected are the *opponens pollicis*, the *abductor pollicis brevis*, and the superficial head of the *flexor pollicis brevis*. The cardinal function of these median muscles is the opposition and abduction of the thumb. In testing the function of the median nerve, we are accustomed to examine first of all the opposition of the thumb, but the following circumstances may detract from the value of this test in lesions at the wrist. First, the *flexor pollicis longus* and the *adductor pollicis*, to some degree, may substitute for the muscles pri-

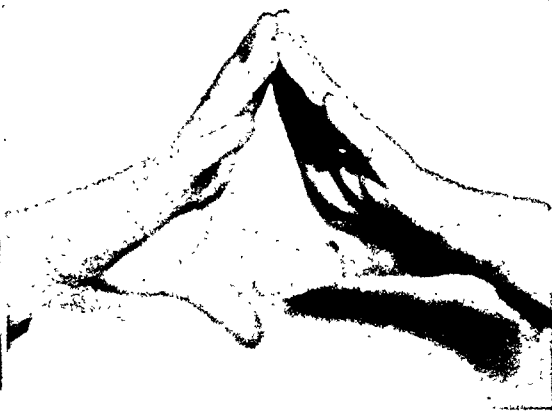
marily responsible for opposition of the thumb. Second, the thenar muscles, which participate in the opposition usually innervated by the median nerve, may be innervated to a varying degree by the ulnar nerve. The compensation by other muscles and the innervation of the median muscles by the ulnar nerve explain why in a lesion of the median nerve at the wrist the opposition of the thumb can be performed remarkably well even if the nerve is completely severed. Third, it is sometimes difficult to determine whether there is real opposition (rotation of the thumb around its own axis) so that the tip of the thumb meets the tip of the little finger or whether there is "pseudo-opposition" in which the thumb meets the radial side of the end phalanx of the little finger. In median nerve lesions at the wrist in which the *flexor pollicis longus* is preserved, this muscle together with the adductors of the thumb (innervated by the ulnar nerve) functions largely in real opposition. Therefore, it would appear *a priori* more advisable in testing the thenar muscles innervated by the median nerve to rely on their function as abductors of the thumb. The ulnar nerve does not participate in the abduction of the thumb. The radial nerve may but it rarely suffers injury together with the median nerve.

This abductor function of the median nerve is too often ignored in textbooks and in monographs on nerve injuries. For example, impairment of the abduction of the thumb as a sign of a median nerve lesion is not even mentioned in the textbook of Bing or in the monographs of Tinel or Stookey.

Our test for a median nerve lesion is performed as follows: The patient is asked to stretch the thumbs of both hands as much as possible, keeping them on a plane with the palm while the other fingers remain adducted. He then is instructed to lift his hands in front of him, as in the position of Oriental prayer, the palms facing the examiner (Fig. 1). In this position the radial tips of the indices touch each other at a horizontal level; so do likewise the tips of both thumbs if there is no lesion of the median nerve. If, however, a median nerve lesion is present, the tip of the thumb of the affected side does not extend horizontally to the tip of the other thumb but instead touches the inner ulnar aspect of the healthy thumb proximal to the tip. The more severe the median nerve palsy is, the more proximally the tip of the affected

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<sup>1</sup>Les nerfs en schémas, p. 518, Paris: Doin, 1925.



Figs. 1 and 2. Median nerve test. Median paralysis on patient's left side. The thumb is held higher than on the

healthy side. The more severe the lesion of the median nerve, the higher the position of thumb, and vice versa.

thumb touches the healthy thumb. A subsiding median nerve palsy is characterized by the ability of the patient to reach more nearly the tip of the healthy thumb with the tip of the affected one. One of my patients who had occupational pressure neuritis of the right median nerve discovered this for himself, and at succeeding monthly visits showed me triumphantly how he could more and more nearly reach the tip of the healthy thumb with the tip of the affected one.

Another technique of this test is as follows: The patient brings his inner fingertips together in a rooflike position at such an angle that the tips of the thumbs maximally abducted at right angles to the palms can touch. If median palsy is present, the tip of the thumb on the affected side is horizontally higher due to deficient abduction (Fig. 2).

This modification is a nearly specific test for affections of the median nerve since abduction of the thumb is the domain of this nerve. The radial nerve co-operates in the abduction of the thumb through the abductor pollicis longus muscle, but a simultaneous involvement of the median and radial nerves is unusual. The ulnar nerve is much less likely to participate in abduction than in opposition. Some deny that the abductor pollicis brevis might ever be innervated by the ulnar nerve.

By this test, which is easy to perform and to interpret, the slightest degree of median nerve weakness can be discovered. It is, furthermore, not only a qualitative but also to a certain extent a quantitative test. It is a good test by which to unmask the malingerer, and an appropriate test for demonstration in neurological teaching.

The test proved to be of particular value in cases of palsy of the ulnar muscles in which it is of paramount importance to rule out even the slight-

est involvement of the muscles innervated by the median nerve. In 3 recently observed cases of atrophy of the ulnar muscles, a concomitant involvement of the median muscles could be clearly demonstrated by this test. Of course, such a finding leads the diagnosis in quite a different direction. The 3 cases mentioned proved to be of the muscular atrophic type and not ulnar nerve paralysis as they seemed to be at first glance.

In median nerve lesions that have been cured by operation or by conservative treatment, the atrophy of the thenar eminence may persist for a long time even after the function of the muscles has become normal. In evaluation of such cases the persistent atrophy may be deceptive because it is muscular function that is most important. The value of the test described lies in the fact that it is a test of function of the muscles supplied by the median nerve. If it is negative, functional recovery is proved despite persistence of some atrophy. This functional restoration can then be confirmed by other tests which show a normal function of median nerve long before the thenar eminence acquires its normal round appearance.

The defective abduction of the thumb in median nerve palsy that constitutes the basis for this test is not easily and clearly evident in the customary examination of a patient with median nerve palsy or by observation of the patient's use of his hands, fingers, or thumbs. Particularly in mild cases, this defective abduction is discernible only by this test in which the patient is made to abduct *ad maximum* his thumb. If the test is negative, i.e., if the tips of the fully abducted thumbs meet at the same horizontal level, it may be concluded that no lesion of median nerve exists, or that complete recovery has occurred.

# DETERMINATION OF PYLORIC PATENCY FOLLOWING THE FREDET-RAMMSTEDT OPERATION FOR CONGENITAL HYPERTROPHIC PYLORIC STENOSIS

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THE Fredet-Rammstedt operation for congenital hypertrophic pyloric stenosis has proved itself one of the most successful procedures in the realm of surgical practice. Donovan's report<sup>1</sup> of 350 consecutive operative cases with one death is evidence of this statement. While many infants are operated upon annually by men who do this operation frequently, still more are probably operated upon by those who do the operation only occasionally. The problem which confronts the occasional operator, as he carries out the technical steps of separating the pyloric musculature, is whether he has actually accomplished relief of the obstruction. He wonders whether he has divided the muscles far enough, he wonders whether the pyloric canal is actually large enough.

Some years ago, as an assistant, I was interested in an infant upon whom the Fredet-Rammstedt procedure was carried out. Following operation, it was evident as time passed that the obstruction had not been sufficiently relieved because the child was still vomiting. Operation was again decided upon and a gastroenterostomy was contemplated. However, when the pylorus was again exposed it was found that the muscles could be separated still further and that the first operation had probably been an incomplete one. In order to avoid such an outcome, in subsequent cases Dr. William A. Fisher suggested making a small incision on the anterior wall of the stomach through which a curved Kelly clamp could be introduced into the pylorus. The jaws of the clamp while in the pyloric canal could be gently spread, giving assurance to the operator that sufficient space was present within the pyloric canal. This maneuver was carried out in a number of cases and worked satisfactorily, especially in convincing the operator that he had attained his original purpose of relieving the pyloric stenosis.

In order to avoid making an incision into the stomach and yet attain the same objective,

namely, assurance that the pylorus was patent, it occurred to me that the tip of a catheter which had already been introduced into the stomach through the nose or mouth could be passed through the pyloric outlet. This principle has been employed in a number of cases with very satisfactory results. As a routine, a No. 10 or 12 French catheter is passed into the stomach through the nose following the anesthetization of the infant with ether. This is done in order to insure an empty stomach and to avoid aspiration of gastric contents on the part of the child. When the separation of the pyloric musculature is completed by the usual method of blunt dissection, the operator identifies the catheter by palpating with his thumb and forefinger through the walls of the stomach (Fig. 1). Manipulation of the tube by the anesthetist will often assist him in finding and directing it. When he secures the catheter in his fingers, the catheter of course lying within the lumen of the stomach and the fingers outside, he passes the tip toward the pylorus. The pylorus meanwhile is held with the fingers of the left hand and with the right hand the tip is directed into and through the pyloric canal. If the tip passes through into the duodenum, the operator can be assured that the pylorus is patent. The catheter can then be partially or completely withdrawn from the stomach depending upon the desires of the operator. In a few instances some difficulty was experienced in finding and manipulating the tube, but usually this was accomplished with ease.

The objection may be raised that this procedure is wholly unnecessary because so many successful cases have been reported without it. The answer to this objection is that the method gives the operator assurance that he has gained his objective, an assurance which he can scarcely have in any other way. If the catheter fails to pass, he can proceed at once to bring about a wider separation of the muscles thereby allowing more space through which the catheter may then be passed. In using this method there has been no evidence of danger, and the soft catheter can hardly be expected to tear the overlying mucosa. Its tip

<sup>1</sup>Donovan, E. J. Congenital Hypertrophic Pyloric Stenosis, *Practice of Surgery*, by Lewis, Vol. 6, chap. 7, p. 5, Harenewtown, Md. W. B. Prior Co., 1910.

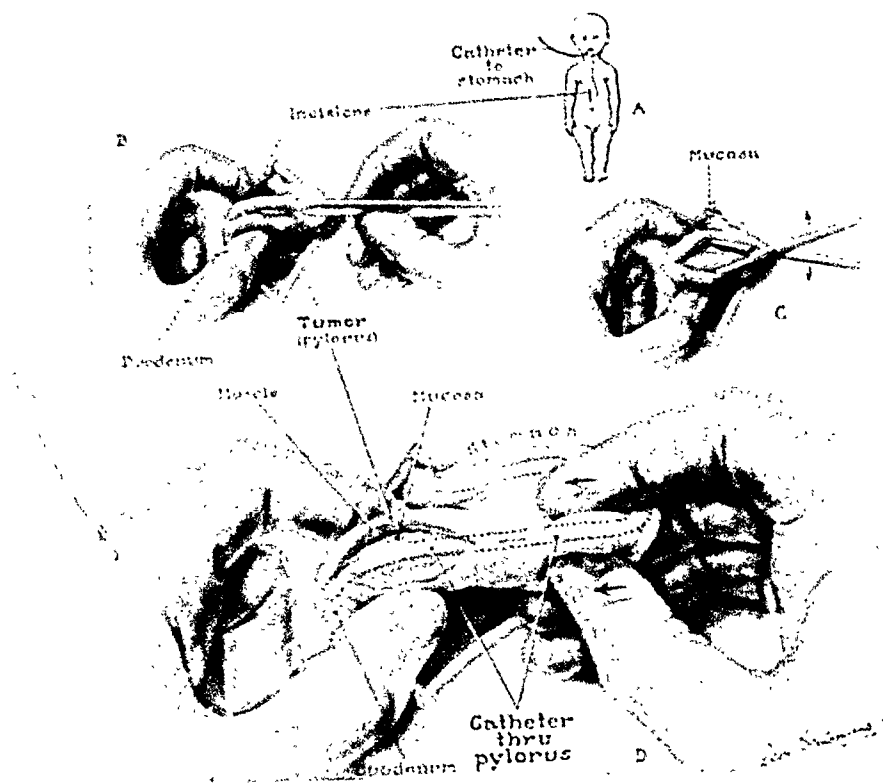


Fig. 1. Method of passing catheter through pyloric canal to determine its patency following the Fredet-Rammstedt procedure.

can readily be seen as it passes, outlined by the mucous membrane. There has never been any suggestion of damage. The method proved especially helpful in 2 cases in which the duodenum had been inadvertently opened at the distal end of the pyloric wound. This accident which happens occasionally is readily remedied by closing the serosa with fine sutures of silk at the point where minute gas bubbles are seen to emerge. In order to be certain that the closure had not caused constriction, the catheter was passed into the

duodenum in each of these cases. This was evidence enough to convince me that the lumen was still sufficient.

This procedure has been used to supplement the Fredet-Rammstedt operation in 8 patients operated upon either by the resident surgeons or myself at the Union Memorial Hospital during the past 3 years. All of the infants have done well and the maneuver suggested here has been considered to be of definite value in the satisfactory completion of the operation.



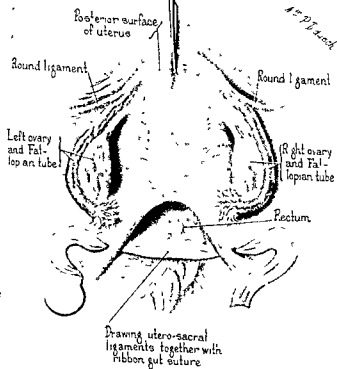
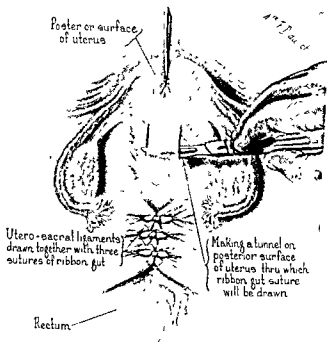


Fig 1. The uterus has been delivered at the abdominal wound. The uterosacral ligaments are drawn together with a ribbon-gut suture studded at one end with an atraumatic needle.

Fig 2. The uterosacral ligaments are snugly drawn together with 3 sutures of ribbon gut. A tunnel is made on the posterior surface of the fundus uteri through which a ribbon-gut suture will be drawn.



# USE OF RIBBON GUT IN UTERINE SUSPENSIONS

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**R**ETRODISPLACEMENT of the uterus is a condition so frequently submitted to surgical intervention, and one for which there are so many methods of correction, that the surgeon often finds himself confronted with the problem of deciding which is the best technique to follow.

Recent considerations of the problem of uterine displacements have impressed gynecologists with the importance of judging each case upon its merits.

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its rather than adhering, routinely, to a particular operative technique. As Crossen aptly remarks: "Most of the symptoms in retrodisplacements are due to complicated conditions. These complications must be recognized and treated if the symptoms are to be relieved. The complications determine to a very large extent the method of treatment to be employed for the displacement."

In those cases of retrodisplacement in which a future pregnancy is possible and the adnexa of both sides are intact and the tissues freely mov-

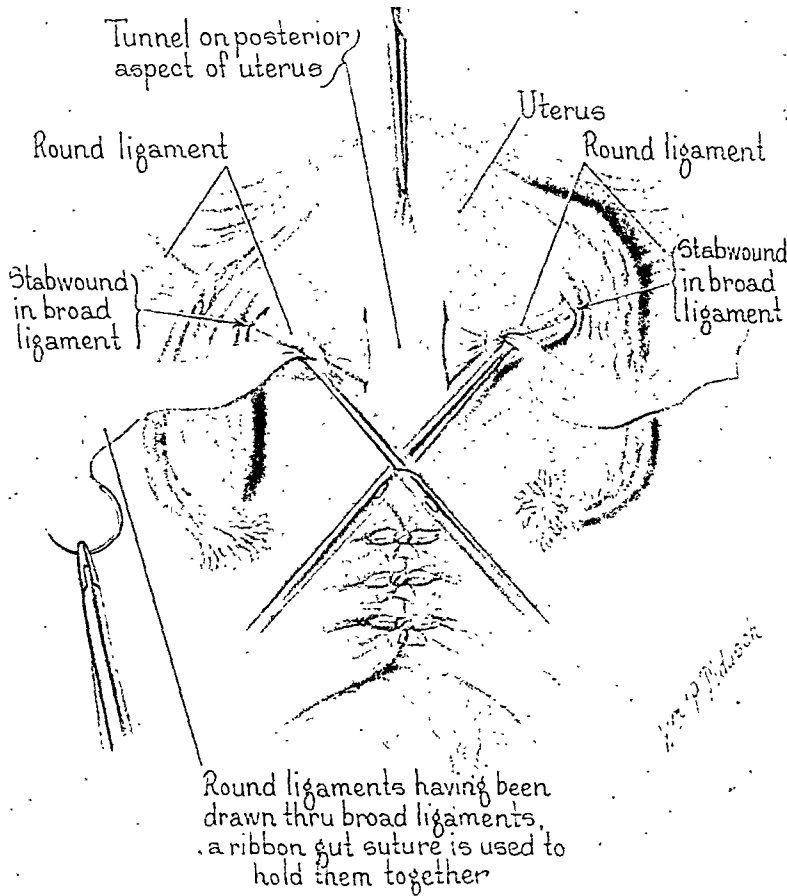


Fig. 3. The round ligaments having been drawn through the broad ligaments, a ribbon-gut suture is drawn through one round ligament, carried through the tunnel, and then through the round ligament on the opposite side.

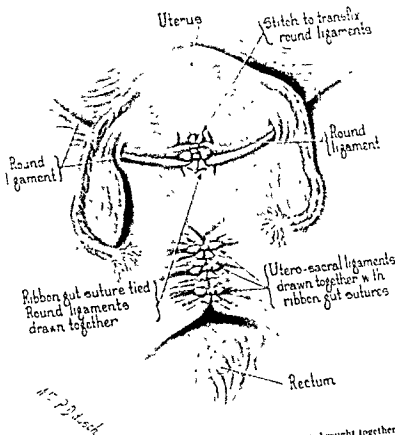


Fig. 4. The ribbon gut suture is tied, and the round ligaments brought together. An extra suture of ribbon gut is placed so as to transfer the round ligaments and the peritoneal covering of the uterus overlying the tunnel.

able, the "posterior implantation of the round ligaments" has been widely used with good results.

The experimental work of O. S. Lowsley (2) on dogs, in which he used chromic ribbon gut in nephropexies, has shown that this material is invaded by fibroblasts which build a strong fibrous tissue bridge on the ribbon. This fact has led Lowsley and his co-workers to use ribbon gut not only in kidney operations but also in other fields of surgery when a sound, strong plastic repair is needed—perineal proctectomy (3), operations for hernia (4) perineal operations, etc. (4, 5, 6). In all of these procedures, ribbon gut has proved highly efficient, and its employment has marked a distinct advance in surgical technique.

The efficiency of ribbon gut in other branches of surgery suggested its use in the operation of

"posterior implantation of the round ligaments" in uterine displacements. It was felt that it would give better support and stronger anchorage to the uterus than are achieved by the use of ordinary catgut or silk.

#### TECHNIQUE OF OPERATION

At the Santo Tomás Hospital, we have been employing the following technique, in those cases in which the uterus is free and movable and the adnexa intact.

The uterus having been delivered at the abdominal wound, the uterosacral ligaments are snugly brought together over the posterior aspect of the uterocervical segment by two or three sutures of chromic ribbon gut studded at one end with an atraumatic needle (Figs. 1 and 2).

With a sharp knife, a tunnel is made on the posterior aspect of the fundus uteri. The round ligaments having been drawn through the broad ligaments, one is transfixed by the ribbon gut, which is carried through the tunnel to the opposite round ligament and tied (Fig. 3). An extra suture of ribbon gut is placed so as to transfix the round ligaments and the peritoneal covering of the uterus overlying the tunnel (Fig. 4).

#### RESULTS

It is too early to draw definite conclusions regarding the real value of this technique in main-

taining the uterus in position, especially after subsequent pregnancies; but it is hoped, and believed, that better results can be expected from the use of ribbon gut than have been obtained by the employment of other suture material.

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# THE EFFECT OF DISTENTION UPON WHOLE BLOOD SPECIFIC GRAVITY AND WHOLE BLOOD POTASSIUM

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THE importance of the rôle played by distention as a factor in the morbidity and mortality of acute intestinal obstruction has recently become increasingly appreciated by both clinical and experimental workers. It is a recognized surgical principle today, that in small intestinal obstruction, decompression of bowel lumen proximal to the site of obstruction, together with a restoration of fluid nitrogen and electrolyte balance, is of the greatest importance.

In a recent review Leigh, Nelson and Swenson were able to show that with the use of the Miller-Abbott tube as an adjunct to surgery of small intestinal obstructions, a mortality of 5.9 per cent was obtained in 68 cases in which the tube was employed, as opposed to previous mortality figures from the same hospital ranging from 66.6 per cent (1916-1919) to 27.6 per cent (1932-1935).

In the voluminous work upon experimental intestinal obstruction, the rôle of distention has received significant comment only during the past decade. Cooper in a comprehensive review of the literature, does not bring up the question of distention *per se*, although he raises 40 pertinent questions in regard to intestinal obstruction.

Herrin and Meek point out that while in 1933 "a toxemia is still generally regarded as the cause of all symptoms, a small group has diverged from this view and presented experimental evidence to show that death from high intestinal obstruction is probably due to non-toxic factors such as dehydration, decrease in blood volume, loss of electrolytes, loss of something specific in the gastrointestinal secretions or alkalosis."

Working with Thiry and Thiry-Vella fistulous loops of the upper jejunum in dogs, they found that "constant distention of the loops with from 50 to 80 millimeters of mercury results in malaise, loss of appetite, excessive secretion from the loops, desiccation and dechlorination of tissues, decreased blood and plasma volumes, increased hemoglobin content, moderately increased alkali reserve, high nonprotein nitrogen and greatly decreased blood chloride."

They felt that the initiating cause of the whole train of symptoms might be the distention of an intestinal segment, and that the loss of chloride was the most serious sequela.

Taylor, Weld, and Harrison stated that "if distention is the primary cause of the sequence of events seen in obstruction, then distention alone should produce the same results as an actual mechanical obstruction." With this hypothesis, they utilized a distensible balloon fashioned around a noncollapsible rubber tube, so that the continuity of the lumen through the distended loop was not eliminated. They found that "most of the animals in which the pressure employed was around 100 millimeters of mercury died within 24 hours with the usual symptoms and postmortem findings of acute obstruction." They observed a close relationship between the severity of symptoms and the degree of distention. They found that in animals which died within 40 hours there was no significant fall in chloride.

They concluded that "distention of the bowel wall is the important factor in the production of the symptoms of experimental intestinal obstruction" and suggested that reflex disturbances effected by afferent nerve stimulation were possibly the significant factor in the train of events.

Fine, Rosenfeld and Gendel, employing the entire ligated small intestine of the cat, to which the extrinsic nerve supply had been eliminated, found that the survival time of the animals was inversely proportioned to the level of pressure in the lumen of the bowel, and that such exclusion of the extrinsic nerve supply did not alter the survival time.

Gendel and Fine, employing the entire small intestine of the dog, found that obstructed dogs which were distended, died more rapidly than simply obstructed dogs, and found that distention of the intestine had a deleterious effect on the general circulation. In distended, obstructed dogs they found an early and progressive loss in plasma volume from 36.4 per cent in 4 to 6 hours to 55 per cent in 24 hours. In this paper as in others they point out that distention *per se* does not effect a significant loss of fluid into the lumen of the gut.

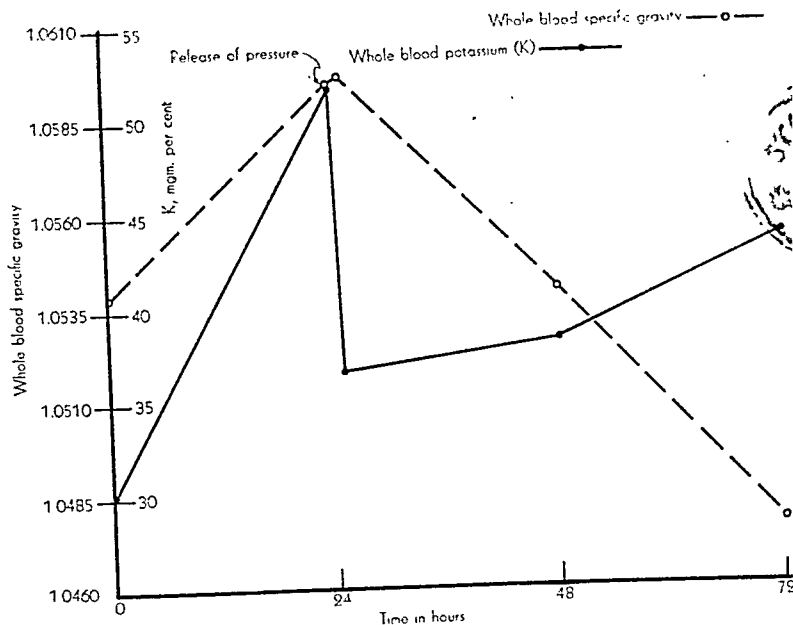


Chart 1. Cat 25. Distention—obstruction without strangulation; pressure, 30 millimeters mercury.

The work cited is in accord with the history that distention greatly aggravates and accelerates, if it is not *per se*, the lethal factor in intestinal obstruction. The modus operandi is not clear. Taylor, Weld, and Harrison did not find chloride loss an early phenomenon. Fine, Rosenfeld, and Gendel found that denervated intestine behaved as did the innervated bowel. Gendel and Fine found a significant loss of plasma volume in distended obstructed intestines in dogs.

Scudder, Zwemer, and Truszowski (7) obstructed the lumen of the intestine of the cat, with tape, at various levels, and followed the condition of the animal to its lethal termination, with

frequent determinations of whole blood potassium and whole blood specific gravity. They found a fluctuating rise in blood potassium to lethal levels, which was preceded by a rise in the blood density.

Many workers have pointed out the analogy in symptoms and signs in such critical conditions as adrenal insufficiency, shock, intestinal obstruction, intestinal fistulas. Scudder (6) has reported blood studies in these conditions and has pointed out the value of determinations of blood density as of value in the guide to therapy.

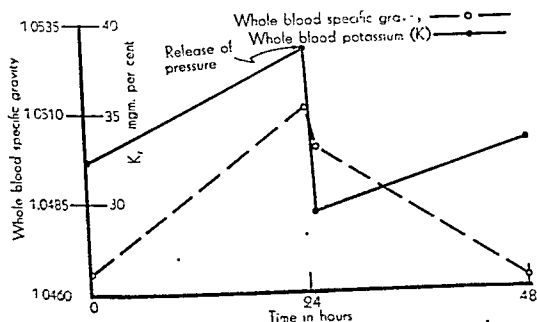


Chart 2. Cat 23. Distention—obstruction without strangulation; pressure, 30 millimeters mercury.

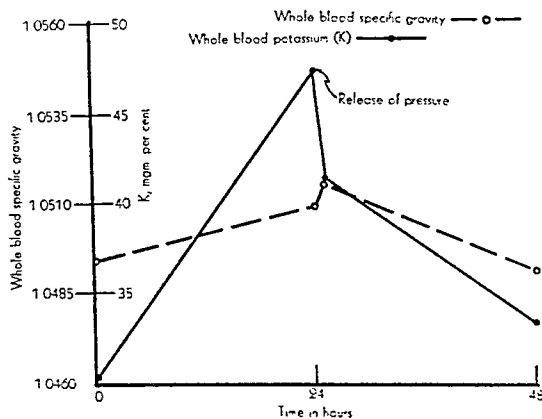


Chart 3. Cat 24. Obstruction—distention without strangulation; pressure, 30 millimeters mercury.

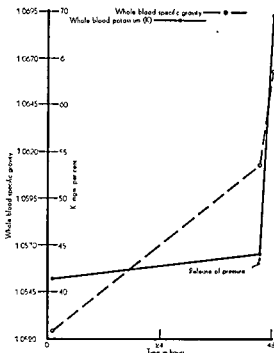


Chart 4. Cat 21. Distention—obstruction with strangulation, pressure, 44 millimeters mercury

In the following experiment the distending pressure was interrupted after varying intervals and concomitant values of whole blood specific gravity and whole blood potassium were recorded. An evaluation of the method of potassium determination with the reservations necessary to its use is discussed by Scudder (6).

Preliminary experiments were carried out on 17 cats to ascertain an effective means of introducing a Miller-Abbott tube into the lumen of the intestine of the cat, to ascertain the most effective distending pressure, which could be used in the balloon, without compromising the blood supply of the wall with subsequent necrosis and perforation, and in determining the effects of this type of distention-obstruction on the bowel of cats.

#### METHOD

The distending medium used was a 16 centimeter condom rubber balloon attached to a No. 14 double lumen rubber tube, similar to the Miller-Abbott (1934) tube. The balloon was introduced through a small opening in the stomach to the desired level in the duodenum, below the ampulla of Vater, the stomach and abdominal wounds were closed around the tube, and the cat was allowed to recover from the ether anesthesia.

It is appreciated that when such a balloon is distended, there is associated obstruction of the lumen of the intestine. The obvious advantage of the method lies in the facility with which the distending pressure may be released, without a second laparotomy.

The cats were fasted for a preliminary 24 hours, so that the small intestine was empty and collapsed. Blood samples were taken from the ear for simultaneous whole blood specific gravity and whole blood potassium determinations, and argenti cobaltonitrite method used for potassium (6).

Blood was taken before anesthesia, 24 hours after distention, 1 hour after release of distention, and 24 hours after release of distention.

When the animal was wide awake after the cessation of ether anesthesia, the balloon was inflated to a pressure of 30 millimeters of mercury. This was accomplished by displacing air from a bottle by the induction of water via a tube from another bottle raised to the height requisite (39 cm.) to register 30 millimeters of mercury pressure on an attached manometer. By using leak proof tested apparatus, the maximum drop in pressure during the duration of the experiments was 1 centimeter of water level.

The distending pressure was then employed for 24 hours, second readings taken, and the pressure released. After one hour a third set of readings was obtained, and 24 hours later a fourth set.

The cats under these conditions suffered the effects of distention and obstruction as witnessed by their appearance of malaise and discomfort, and by the vomiting of bile-stained duodenal contents. They were given no water nor parenteral fluid during this time.

Charts 1, 2, 3 illustrate the changes in the values of blood potassium and whole blood specific gravity which accompanied distention of the lumen of the duodenum of the cat by the method described. The distending pressure was maintained for 24 hours, and then released. In these instances, at the end of 24 hours of distention there was a marked elevation of whole blood potassium and a similar marked rise in the whole blood specific gravity. An hour after the release of the distending pressure there was an appreciable fall of whole blood potassium toward the base level, and a subsequent fall in whole blood specific gravity. At autopsy, when the animals were killed, no compromised loops of bowel were found.

Charts 4 and 5 show the changes in two cats in which the distending pressure was higher, 44 millimeters of mercury, and in which the pressure was maintained for 48 hours. At the end of 48

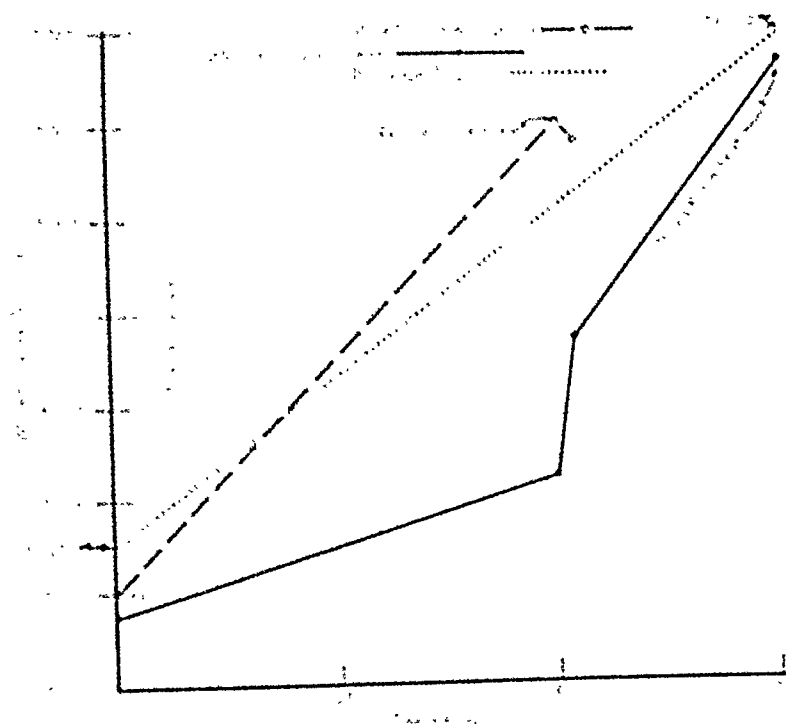


Chart 5. Cat with intestinal distention with strangulation; pressure, 44 millimeters mercury.

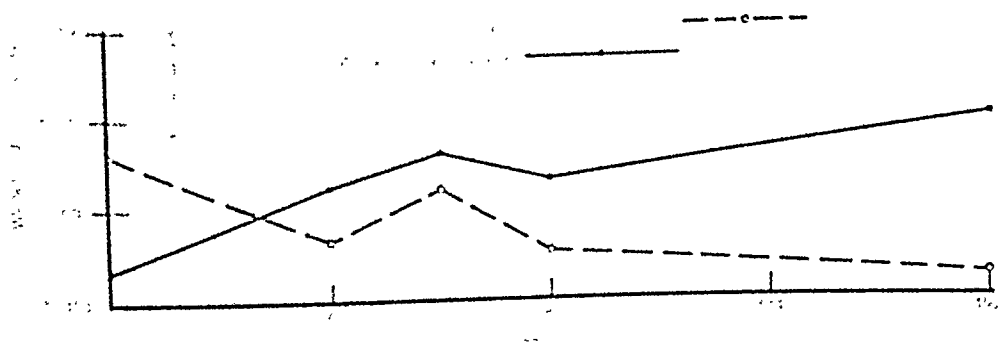


Chart 6. Control cat. Balloon not inflated.

hours there was an elevation in whole blood potassium and a marked elevation of whole blood specific gravity. An hour following release of the pressure there was instead of a fall of these values (Chart 4) a striking rise, as shown. The animal died 1½ hours after the release of pressure and a gangrenous loop of duodenum was found.

Chart 5 shows the same rise in potassium after 1 hour and a transient drop in whole blood specific gravity. The subsequent rise at the end of 72

hours is shown. The animal died at 72 hours and a gangrenous loop of duodenum was found.

Chart 6 illustrates the values in a cat in which the balloon was introduced but not inflated.

#### CONCLUSIONS

Following 24 hours of distention of the duodenum of the cat there is an elevation of peripheral whole blood potassium and whole blood specific gravity.



One hour following release of the distending pressure, there is a fall in whole blood potassium and at the end of 24 hours following release of distention there is a continued fall in potassium and a fall in whole blood specific gravity. These values are recorded in animals without fluids.

Following 48 hours of distention with a higher pressure there is an observable rise in both of these values.

Following the release of the distending pressure for such a time, the combination of which is sufficient to produce a gangrenous loop, the values abruptly rise to the lethal termination.

In the first instance, i.e., in distention of short duration without compromise of bowel, the process is reversible; in the second, i.e., the longer period of distention with compromise of bowel,

the release of the distending pressure is accompanied by an increase in the hemoconcentration and rise in potassium.

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ant method of administering concentrated bile or purified bile salt is more effective, since adequate concentrations of bile salts are assured. It is usual for patients with severe disease of the extrahepatic biliary tract to have a deficiency of bile salt in the bile, and it is wise to supplement this. In addition, the added cholerisis resulting tends to aid in flushing out the common duct and decreases the amount of sediment found.

Bile salt or whole bile administered to patients with gall stones is palliative treatment and cannot be relied upon for permanent relief. As an adjunct to surgery, bile therapy is important before operation to help in restoring or maintaining an adequate prothrombin level and in adding to the comfort of the patient. After operation, restoration of bile salt in the patient's own bile by the administration of bile from animals affords a physiological means of restoring to normal the disturbed digestive processes resulting from deficiency in the patient's own bile.

CHARLES G. JOHNSTON

## BLOOD PLASMA PROTEINS

**P**OINTS of view relative to plasma proteins have been changing rapidly during the past 10 years. It is fair to say that 20 years ago physicians looked upon the plasma proteins as inert materials having to do with osmotic pressure but not concerned with the internal protein metabolism of the body. Many believed that they could be replaced adequately by inert materials such as gums, for example, acacia.

Experimental work has brought many facts to light which indicate that the physician must know more about plasma proteins. Their importance in the next few years will probably increase rather than diminish and their study will be of corresponding interest to surgeons

and physicians. Much research work with animals and careful study of clinical cases are being published, and this trend undoubtedly will increase.

It is our belief that the plasma proteins take an active part in the internal protein metabolism of the body, that they are built up rapidly, used in the body economy freely, and serve to supply practically all of the protein requirements of the cells of the body. Evidence is at hand to show that a healthy dog can produce a maximum of about 1 gram of plasma protein per kilogram body weight per day, and it is probable that the human being under favorable circumstances can do something of the same order. This means that a 70 kilogram dog can produce 70 grams of new plasma protein a day, which amounts to about a third of his circulating plasma protein, a turn-over, let us say, of 30 per cent being a distinct possibility.

A dog may be maintained in nitrogen equilibrium, weight equilibrium, and in health by injecting protein in suitable amounts as dog plasma while feeding only fat, carbohydrate, salts and accessories. This plasma protein given by vein obviously supplies all the requirements of the healthy animal over periods of many weeks. If this can be done in such an emergency, it probably is done more or less continuously in health. It seems likely that this plasma protein supplies the protein requirements of the various cells of the body, organs, muscle, and interstitial tissue. Many of the plasma proteins are believed to be formed in the liver, although a few of the globulins undoubtedly are formed outside of the liver. The liver, therefore, is the great factory which produces this actively metabolized protein for use throughout the body.

There are many occasions when use of plasma protein concerns the surgeon and physician. Any form of hypoproteinemia may



# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

A BRITISH text *A Practical Manual of Diseases of the Chest*<sup>1</sup> first appearing in 1935, is now in its second (1941) edition. The material has been extensively revised and the chapter bibliographies contain many recent references.

This treatise reports in a practical, didactic fashion both the medical and surgical aspects of most of the chest disease problems encountered.

The introductory 4 chapters of the volume consider a fundamental study of the anatomy, physiology, radiology and physical diagnosis related to the respiratory system. The 32 remaining chapters are devoted to a clinical review of most of the common and rare chest diseases. These are included in groups divided by clinico-anatomical regions as follows: diseases of the upper respiratory tract—nasopharyngitis, laryngitis; diseases of the lower respiratory tract—bronchitis, bronchiectasis, foreign bodies; asthma; pleural diseases; diseases of the lung—collapse, emphysema, pneumonia—37 pages; tuberculosis—124 pages; intrathoracic suppuration; new growths; and miscellaneous—differential diagnosis, mediastinal disease, oxygen therapy, prescription formulary.

The presentations are well illustrated by numerous clear x-ray reproductions, charts, photomicrographs, and drawings; there are about 200 such. Sixty-two well chosen case histories from the files of the Brompton Hospital are cited to portray the practical clinical problems.

As is to be expected in a volume by a single author, much more emphasis is placed on certain disease entities than others. The author in writing of diseases with which he is less familiar has obtained the best opinion presented in available literature and presents his conclusions on these phases.

The major respiratory disease problems are efficiently treated. This manual is a valuable asset to the library of the student of medicine, as a text for the undergraduate or a reference work for the busy practitioner.

EUGENE L. WALSH.

THE comparatively brief book *The Pharmacology of Anesthetic Drugs; A Syllabus for Students and Clinicians*<sup>2</sup> by John Adriani presents by means of diagrams, schematic drawings and tables, a digest of the properties, actions, and techniques of administration of the anesthetic agents, both for general

anesthesia and local anesthesia, as well as of various auxiliary agents. The method of presentation is therefore not well suited to casual reading, but would probably be of value as a teaching manual in a course devoted to anesthetics. The title of the book might be interpreted by many clinicians to signify that it is primarily devoted to the basic and fundamental problems of anesthesia and anesthetic agents. This is not the case, as it is most concerned with the items of interest to the practicing anesthesiologist and surgeon. The method of presentation necessitates a rather dogmatic treatment, but the author has been as judicious in this respect as the method would permit.

CARL A. DRAGSTEDT

THE book of Samson Wright on *Applied Physiology*<sup>3</sup> has represented an outstanding contribution to texts in the field of physiology since the first edition. This seventh edition represents a marked improvement. So much new material has been added that practically every chapter has been enlarged and improved. Practically every advance made in physiology in recent years, of importance to the physician and to the student of medicine, is included. The book unquestionably exemplifies the importance of physiology in the practice of medicine and how the recognition of this fact has grown in recent years. The book is recommended to students and practitioners of medicine without reservation.

A. C. IVY.

THE third volume of the four-volume work on therapeutics edited by Blumer<sup>4</sup> with a number of contributors has recently appeared. The material covered includes diseases due to fungi, metazoan and protozoan diseases, intoxications, diseases due to physical agents, treatment of edema, dehydration, acidosis and alkalosis, preoperative and postoperative treatment, treatment of diseases of the lower respiratory tract, treatment of diseases of the blood and lymph vessels, and treatment of heart disease.

This volume continues to present in a stellar manner the basic underlying treatment. In fact the work improves with each succeeding volume. As in previous sections there is some duplication. For instance scorpion poisoning is described in two chapters, incidentally with disagreement as to the production of scorpion antivenin.

<sup>1</sup>A PRACTICAL MANUAL OF DISEASES OF THE CHEST. By Maurice Davidson, M.A., M.D. (Oxon), F.R.C.P. (Lond.) 2d ed. London and New York, Oxford University Press, 1941.

<sup>2</sup>THE PHARMACOLOGY OF ANESTHETIC DRUGS. A SYLLABUS FOR STUDENTS AND CLINICIANS. By John Adriani, M.D. 2d ed. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1941.

<sup>3</sup>APPLIED PHYSIOLOGY. By Samson Wright, M.D., F.R.C.P. 7th ed. New York: Oxford University Press, 1940.

<sup>4</sup>THE THERAPEUTICS OF INTERNAL DISEASES. Edited by George Blumer, M.A. (Yale), M.D. With the assistance of Albert J. Sullivan, M.D. Vol. 3. New York and London: D. Appleton-Century Co., Inc., 1941.

Contributors continue to be prominent specialists well qualified in the various fields. Particularly noteworthy are chapters by the senior author on intoxications, treatment of diseases of the blood and lymph vessels by Wright, and treatment of heart disease and heart failure by Marvin. While titled *The Therapeutics of Internal Diseases*, this work is developing into an excellent treatise on medicine with special emphasis on treatment.

JAMES R. MILLER.

SINCE its first edition in 1915 *First Aid in Emergencies*<sup>1</sup> by Eldridge L. Eliason has enjoyed wide distribution. This 260 page, pocket-size book is designed for police, firemen, boy scouts, and many other lay groups. The tenth edition has been completely revised and reset and illustrated with 126 halftone and line drawings. Resetting has been typographically satisfactory but the revision has not rejuvenated an aging volume. For example, the author recommends the use of laudanum or lead water, or both, to laymen for such widely varying conditions as contusions, insect wounds, sprains, dislocations, fractures, corrosive acid poisoning, asthma, earache, and hives; and apparently does not realize that no layman is able to purchase laudanum legally within the United States since it is subject to the rules and regulations of the Narcotic Act.

His recommendations in the treatment of dislocations by laymen are open to question. For example in the treatment of dislocation of the shoulder the directions state: "Send for a physician. If one is not obtainable, then you may try reduction." Then he describes for the layman the hazardous technique used in the Hippocratic period of placing the foot in the axilla with progressive traction on the arm, and

erroneously refers to Figure 50. At no point is there any caution of possible fracture-dislocation or damage to axillary vessels and nerves. Under dislocation of the elbow in describing the deformity and illustrating it, the author states "Reduction is usually left to a physician" and then describes how it should be done showing a halftone illustration of a husky, shirt-sleeved individual reducing an elbow fracture across the knee after the method described by Sir Astley Cooper.

In describing "carriage in supine position" the description states all three bearers kneel, each on one knee (the knee nearest the patient's feet) and then shows two illustrations showing all three bearers kneeling on the knee nearest the patient's head.

An undesirable illustration shows the obsolete technique of elevation of a patient's pelvis for "emptying water from the lungs." This technique has long been discontinued as it is inadequate and delays the beginning of revivification procedures.

Under foreign bodies of the eye, among the directions to laymen are, "If the particle is easily seen and a physician is not available, gentle attempts may be made to dislodge it with a sterile needle point. A drop of 1 per cent cocaine solution in the eye one minute before attempting removal helps." These directions are for laymen.

The woefully incomplete index which presumably would be used in emergency does have an entry for botulism but no entry for food poisoning; no entry under bites; no entry under dog or dog bites—yet it does index Gila monster. There are many similar but perhaps minor criticisms that might be added.

This handy volume, bound in a semiflexible water resistant cover, contains many interesting descriptions and illustrations but could be recommended only to the highly critical reader and certainly not to the average inexperienced novice who wishes to be helpful in an emergency.

FELIX JANSEY.

<sup>1</sup>First Aid in EMERGENCIES. By Eldridge L. Eliason, A.B., M.D. Sc.D., F.A.C.S. 10th ed. Philadelphia, Montreal, and London: J. B. Lippincott Co., 1941.

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

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